South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde
P.O. Box 643, Cape Town Posbus 643, Kaapstad

Cape Town, 5 January 1957 Vol. 31 No. 1 Kaapstad, 5 Januarie 1957
Weekly 2s. 6d. Weekliks 2s. 6d.

VACCINATION AND VIRUS DISEASES DURING PREGNANCY

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Since the original description by Gregg[1] in 1941 of the relationship between congenital cataract and maternal rubella there has been increasing interest in the effects on the foetus of virus diseases and other diseases in the mother during pregnancy.

In this paper an investigation into the effects of vaccination against smallpox is reported, and the influence of viruses generally is reviewed.

VACCINIA

Many authors—Gast,[2] Vignes[3] and others—have stated that vaccination does not affect the mother adversely, nor does it interrupt the pregnancy. Bellows, Hyman and Merritt[4] found very little difference in the incidence of abortions, stillbirths, neonatal deaths and congenital malformations in a group of 893 vaccinated and 173 non-vaccinated patients. Greenberg[5] reported no differences with regard to malformations in a group of 2,791 cases, of whom 364 were vaccinated in the first trimester, 688 in the second and 927 in the third.

MacArthur,[6] on the other hand, obtained different results. He studied (by questionnaire) 203 patients who had a reaction to vaccination during pregnancy, 67 in the first trimester, 69 in the second and 67 in the third. He found that 47% of the patients who had a positive reaction between the 4th and the 12th weeks of gestation failed to give birth to a healthy child. Thus in 34 cases 17 babies were normal and 1 premature, while there were 10 abortions, 5 stillbirths and 1 foetal abnormality. The corresponding foetal loss in the first month, the second trimester and the third trimester respectively was 3%, 3% and 2%. The same author describes the case of a patient who had a severe reaction to vaccination at 12 weeks' gestation. Three months later she delivered spontaneously a feeble hydropic premature infant with severe generalized vaccinia (nuclear inclusion bodies were found at post-mortem). Vaccinia in the foetus was described by Lynch[7] 20 years earlier—in 1932.

In mid-December 1955 there were a few cases of smallpox in Cape Town and the population was advised to be vaccinated. Among those vaccinated were many pregnant women and thus a very favourable opportunity was provided to study its effects.

The incidence of stillbirths, neonatal deaths and congenital malformations was studied in 1,121 patients who had been vaccinated during the first 20 weeks of pregnancy and in 201 controls who had not been vaccinated during their pregnancy. The vaccinated patients were divided into 510 'positive' and 611 'negative'. The 'positives' were those who stated that a blister had formed and had been followed by the separation of a scab. No search was made for the scar, because it could easily be confused with a scar resulting from vaccination on a previous occasion. The results of the investigation are shown in Table I, in which the patients are classified in 3 groups, viz. (1) 'positive' vaccinated, (2) 'negative' vaccinated, and (3) not vaccinated.

TABLE I

Vaccination	*Total*	*Still-births*	*Neonatal Deaths*	*Congenital Abnormalities*
Positive	510	11 (2·1%)	7 (1·2%)	8 (1·5%)
Negative	611	10 (1·6%)	8 (1·3%)	16 (2·6%)
Not vaccinated ..	201	3 (1·5%)	3 (1·5%)	3 (1·5%)

These results are in accordance with the findings of Bellows *et al.*[4] and Greenberg[5] that there is no increase amongst the vaccinated in the incidence of stillbirths, neonatal deaths or congenital malformations; and do not support MacArthur's view that there is a higher foetal loss in patients vaccinated between the 4th and 12th weeks of gestation.

Unfortunately a forward type of investigation of the abortion rate could not be made, because the vast majority of patients in the institutions book after 12 weeks and many may thus have aborted before they could book. In cases treated privately it seems that the majority were advised not to be vaccinated at that stage

of pregnancy. In 6 patients, however, who were seen before vaccination, and who had a positive response to vaccination between the 4th and 12th weeks, all had normal deliveries, 1 baby being premature.

RUBELLA

Rubella, which was previously considered to be one of the mildest of the exanthemata, has in the past 15 years loomed up as a major catastrophe of early pregnancy. Unfortunately, it is at its most infective before the appearance of the rash.

There is wide divergence of opinion regarding the frequency of abnormality following maternal rubella in early pregnancy. This may to some extent be accounted for by the method of collecting cases. Retrospective enquiries yield a high incidence. Swan[8] claimed that it was as high as 74% when rubella occurred in the first 4 months of pregnancy. Abel and van Dellen[9] studied 82 cases. Of 81 living children, 25 were normal and 56 were abnormal. In this series 87% of patients who had rubella in the first trimester had abnormal babies, and 42% in the second trimester. Anderson[10] found that of 44 women who had rubella in the first trimester, 22 had children with defects, whereas only 3 of 22 who had it in the second trimester had defects, and 2 of 14 in the third trimester. Fox and Bortin[11] collected 11 patients who had had rubella during pregnancy (9 in the first 4 months). There was only 1 abnormality, a hydrocephalic. Swan[12] collected 939 cases of congenital abnormality following rubella and 220 cases in which the babies were normal. Among the latter were 111 in whom the illness was contracted in the first 4 months of pregnancy.

Types of Abnormalities. The parts chiefly affected are the eyes (causing cataract), the inner ear (causing deaf-mutism) and the heart (mostly as patent ductus arteriosus and septal defects). In Swan's series there were 435 cases of cataract, 400 deaf-mutes, 403 cases with cardiac defects, 164 cases of microcephaly and 126 cases of mental deficiency. There were many other minor miscellaneous abnormalities. It will be seen that a very large proportion of the malformations are not amenable to treatment.

Pathogenesis

There are 2 hypotheses:

1. That the virus penetrates the barrier between the mother and the foetus and attacks the foetus directly.

2. The indirect theory of Gillman *et al.*,[13] who believe that the virus evokes a metabolic disorder, primarily of the mother and secondly of the foetus. By injecting varying amounts of trypan blue into rats they were able to produce a varying incidence of abnormality.

A few patients who have had pre-conceptional rubella have been found to have defective children. Swan [12] quotes 5 such cases. He believes that the virus has possibly persisted in the tissues of the original host and become re-activated with the advent of the embryo with more susceptible cells. If the indirect hypothesis is accepted, possibly the abnormal maternal metabolic state has persisted. Patients should therefore be advised not to become pregnant for a while after they have recovered from rubella.

At least 40 cases are known in which an immune mother has been exposed to smallpox and the foetus has developed smallpox in utero.[14] Schick believes that this is due to the fact that the viruses are able to pass through the placenta, but that the antibodies are not. There is no apparent reason why this state of affairs should not exist with rubella. Hagstromer[15] quotes 2 cases in which immune mothers were exposed to measles in the first month of pregnancy. Both had deformed children, one with a cleft palate and a rudimentary ear and the other a cleft palate.

The Problem

Numerous problems arise in dealing with cases of rubella in early pregnancy:

1. Did the patient actually have rubella? Mild cases can easily be missed and in some the differentiation from glandular fever may not be possible.

2. Should the patient be informed of the risks to which her foetus has been exposed? Today it is common knowledge and she will almost certainly find out. The risks are unquestionably high, as shown in almost every series published, and surely she is entitled to know about it. This knowledge, however, will produce grave anxiety and in many cases a psychiatric problem. One will surely not be blessed when the unfortunate patient who has a defective infant discovers that the prognosis was known all along to be grave and that no steps were taken to meet the situation.

3. Should therapeutic abortion be performed? Almost every doctor has been faced with this problem. I have no doubt that each case has been given anxious thought before a line of action has been adopted one way or another. On the one hand is the fear of a grossly defective child, a heavy burden to any family, and on the other is the fear of destroying a perfectly healthy foetus. Some will consider it callous not to terminate pregnancy, whereas others will consider it callous to do so. It is really a point of view, based, as Greenhill[16] states, on statistical considerations. Legally, the only indication for termination is the psychiatric aspect. In the case of Rex v. Bourne the judge stated that 'if pregnancy is likely to make a woman a physical and mental wreck a doctor who operated in that belief did so for the purpose of preserving the life of the mother'. It is submitted that this interpretation of the law might also be accepted in South African courts.[17] There is obviously no physical danger to the mother. In answer to a questionnaire sent by Caldwell and Whitener[18] to medical schools, 25 replies were conservative, and in 11 schools the practice was to explain the position to the patient and offer therapeutic abortion. The subject is freely discussed in the lay press, and may produce a grave psychological state in the pregnant woman. Termination may be justifiable in such cases.

Preventive Measures

1. Rubella camps for young girls have been suggested. There is always the danger of pregnant women contracting the disease in these artificial epidemics.

2. With regard to isolation, it is unfortunate that the illness may have been spread before the appearance of the rash, and thus before diagnosis may have been possible.

3. Passive immunization with gamma globulin is possibly helpful. In 133 children exposed, 6 c.c. of gamma globulin was administered and only 6 developed rubella. In a control group of 129 exposed children 22 developed rubella.[14] In Australia a special gamma globulin is prepared from convalescent rubella patients. Of 570 women exposed who received it, 7 developed the illness. It is hoped that it will not be long before active immunization can be conferred in rubella as in smallpox and yellow fever. It will indeed be a great advance, which may go far to solve the whole problem.

Other Viruses

Other virus diseases occurring in pregnancy may also cause congenital malformation, although to a lesser degree than rubella. Statistics from various authors are collected in Table II.

TABLE II

Virus Infection	*Total*	*Congenital Malformations*	*Normal*
Measles			
Swan[12]	62	11	47
Packer[23]	18	2	
Chicken-pox			
Swan[12]	29	5	22
Herpes Zoster			
Swan[12]	3	2	1
Mumps			
Swan[12]	93	18	68
Schwartz[24]	11	0	10
Infective Hepatitis			
Swan[12]	31	3	22
Mansell[25]	21	5	
Poliomyelitis			
Swan[12]	195	6	141

The question will arise whether poliomyelitis vaccine should be administered to pregnant women, as it is thought that the risk of contracting this illness during pregnancy is slightly increased. Priority rating has been given for the Salk vaccine.[19]

In an influenza epidemic in Ireland in 1950-51, Campbell[20] found that 164 of 989 pregnant women contracted influenza. There was no difference in the stillbirth rate nor the abnormality rate in the two groups.

The virus causing rubella thus remains the chief offender, although others may cause much concern. On statistical evidence Horowitz[21] claims that maternal rubella is responsible for 4·2% of congenital abnormalities. Grönvall and Selander[22] studied the histories of 354 Swedish mothers with defective children and found that in 5% of these women virus diseases had occurred during pregnancy. Thus, although Gregg's observations have shed some light on the causes of these fascinating and pathetic malformations, we are still to a large extent groping in the darkness. When one considers the myriads of delicate embryological developments which occur between conception and the birth of the child, one can only marvel at the fact that malformations are as rare as they are.

SUMMARY

The effect of vaccination against smallpox on the incidence of stillbirths, neonatal deaths and congenital malformations was studied in 1,121 patients and compared with 201 controls. It appears that vaccination during pregnancy is not contra-indicated.

The problem of rubella during pregnancy is discussed, particularly in relation to the abnormality rate, the varieties of abnormality, the pathogenesis, preventive measures and management.

The incidence of malformations in other virus diseases is mentioned.

I wish to thank Prof. James T. Louw for allowing me to carry out this investigation and for his keen interest, assistance and advice; Dr. David Friedlander for his suggestions and keen interest; the Superintendents of the Somerset, Peninsula Maternity, Mowbray Maternity and St. Monica's Hospitals and the Matron of the Salvation Army Maternity Hospital, for their kind cooperation. I wish, too, to thank the registrars and house surgeons and all my other colleagues who have so willingly given assistance.

REFERENCES

1. Gregg, N. McA. (1941): Trans. Ophthal. Soc. Austral., **3,** 35.
2. Gast, A. Cited by Bellows *et al.*, *loc. cit.*[4]
3. Vignes, H. (1942): Presse Méd., **50,** 364.
4. Bellows, M. T., Hyman, M. E. and Merritt, K. K. (1949): Pub. Hlth. Rep. (Wash.), **64,** 319.
5. Greenberg, M. (1949): Pediatrics, **3,** 456.
6. MacArthur, P. (1952): Lancet, **2,** 1104.
7. Lynch, F. W. (1932): Arch. Derm. Syph. (Chicago), **26,** 997.
8. Swan, C. Cited by Lemmon, W. M. (1950): Med. J. Austral., **2,** 392.
9. Abel, S. and van Dellen, T. R. (1949): J. Amer. Med. Assoc., **140,** 1210.
10. Anderson, S. G. (1950): Med. J. Austral., **2,** 389.
11. Fox, M. J. and Bortin, M. M. (1946): J. Amer. Med. Assoc., **130,** 568.
12. Swan, C. In Banks, H. S. (1951): *Modern Practice in Infectious Fevers,* vol. 2, p. 528. London: Butterworth.
13. Gillman, J., Gilbert, C. and Gillman, T. (1948): S. Afr. J. Med. Sci., **13,** 47.
14. Murray, H. B. (1952): Advanc. Intern. Med., **5,** 15.
15. Hagstromer, A. (1948): Acta paediat. (Uppsala), **35,** 242.
16. Greenhill, J. P. (1952): Year Book of Obstet. and Gynec., 275. Chicago: Year Book Publishers.
17. Rhodes, W. F., Gordon, I. and Turner, R. (1942): *Medical Jurisprudence,* 1st ed., p. 66. Cape Town: Stewart Printing Co.
18. Caldwell, J. B. and Whitener, D. L. (1951): N. Carolina Med. J., **12,** 104.
19. Bates, T. (1956): Obstet. Gynec. Surv., **11,** 86.
20. Campbell, W. A. B. (1953): Lancet, **1,** 173.
21. Horowitz, J. (1950): Arch. Pediat., **67,** 364.
22. Grönvall, H. and Selander, P. (1948): Nord. Med. (Stockholm), **37,** 409.
23. Packer, A. D. (1950): Med. J. Austral., **1,** 835.
24. Schwartz, H. A. (1950): Amer. J. Obstet. Gynec., **60,** 875.
25. Mansell, R. V. (1955): *Ibid.*, **69,** 1136.

Suid-Afrikaanse Tydskrif vir Geneeskunde

South African Medical Journal

EDITORIAL

CANCER

Some of the developments that have taken place in the field of cancer research in the past few years have recently been authoritatively reviewed in a useful article by Mider[1] in the *Journal of Chronic Diseases*. The article contains 159 references. The attacks that have been made from the clinical and laboratory angles to solve this grave problem are indicated, and tribute is paid not only to the research workers but also to the pharmaceutical industry and the public for their valuable support.

Perhaps not sufficient of the energy expended in cancer research is devoted to investigation of the causation of the disease. There are naturally many difficulties. It takes a long time to produce cancer with most carcinogenic agents, of which there is a great number, with variation in chemical structure. Much depends on the experimental animals used and on their resistance and their susceptibility to induced cancer. The observations on carcinogenesis in special strains of laboratory animals may assist in the recognition of groups of patients prone to develop one or other specific type of cancer, but advances along these lines will be slow. The observation of particular kinds of cancer among the population may assist in the discovery of causal agents that can be eliminated from the environment. It is interesting to note that 'only six clearly identifiable agents are known to cause cancer in man: (1) X-rays and some of their constituent parts (it matters little whether generated by machines or by artificially-induced or naturally-occurring radio-active substances provided experimental data are correct), (2) ultraviolet irradiation, (3) arsenic, (4) beta-naphthylamine, (5) benzidine, (6) 4-aminodiphenyl.'

These chemical compounds, or others still to be recognized, are presumably present in the various substances that have been incriminated as carcinogenic agents in man, such as soots, shale oils, paraffins, and other materials encountered in certain occupations. The increase in the incidence of primary carcinoma of the bronchi and lungs is of greater interest in view of the suspected relationship between certain environmental factors and this type of neoplasm. So great is

VAN DIE REDAKSIE

KANKER

Sommige van die ontwikkelings wat gedurende die afgelope paar jaar op die gebied van kankernavorsing plaasgevind het, is onlangs met gesag in 'n nuttige artikel deur Mider[1] in die *Journal of Chronic Diseases* hersien. Die artikel bevat 159 verwysings. Die aanvalle wat van uit die kliniese en laboratoriese gesigspunte geloots is om hierdie ernstige probleem op te los, word aangedui en hulde word nie alleen aan die navorsers betoon nie, maar ook aan die farmaseutiese industrie en die publiek vir hulle waardevolle steun.

Miskien word nie genoeg van die energie wat aan kankernavorsing bestee word, aan die ondersoek van die veroorsaking van die siekte gewy nie. Daar is natuurlik baie moeilikhede. Dit duur 'n lang tyd om kanker met die meeste van die karsinogeniese verwekkers, waarvan daar 'n groot aantal met afwissellende chemiese struktuur is, voort te bring. Baie hang van die eksperimentele diere af wat gebruik word, en hulle weerstand en onderhewigheid aan opgewekte kanker. Die waarnemings by spesiale rasse van laboratoriumdiere i.v.m. die oorsprong van kanker, mag help om groepe van pasiënte wat geneig is om een of ander spesifieke tipe van kanker te ontwikkel, te herken, maar vooruitgang in hierdie rigting sal stadig wees. Die waarnemings van besondere tipes van kanker onder die bevolking mag help by die ontdekking van veroorsakende verwekkers wat van die omgewing uitgesluit kan word. Dit is interessant om daarop te let, dat dit bekend is dat slegs ses duidelik herkenbare stowwe kanker by die mens veroorsaak: (1) X-strale en sommige van hulle samestellende dele (dit is van weinig belang of dit deur masjiene, of deur kunsmatig-opgewekte, of radio-aktiewe stowwe wat natuurlikerwys voorkom, voortgebring word, mits eksperimentele gegewens juis is), (2) ultraviolet bestraling, (3) arseen, (4) beta-naftielamien, (5) bensidien, (6) 4-aminodifeniel.'

Hierdie chemiese verbindings en andere wat nog herken moet word, is oënskynlik aanwesig in die verskeie stowwe wat daarvan beskuldig is dat hulle karsinogeniese verwekkers by die mens is, soos byvoorbeeld, roete, skalie-olies, paraffiene, en andere stowwe wat by sekere beroepe aangetref word. Die toename in die voorkomssyfer van primêre karsinoom van die lugpype en longe is van groter belang weens die verdagte verwantskap tussen sekere omgewingsfaktore en hierdie tipe van neoplasma. Só groot is die voorkomssyfer en verspreiding van hierdie siekte, dat die karsinogeniese verwekker wyd versprei moet wees. Die navorsings i.v.m. die verband tussen die rook van tabak en long-

the incidence and distribution of this disease that the carcinogenic agent must be wide-spread. The investigations on the association between tobacco smoking and pulmonary cancer are considered by the author. He puts forward the possibility that pulmonary cancer may be produced by agents excreted through the lungs but entering the body by extra-respiratory channels; there is much evidence that carcinogenic agents may act at a distance from their entry to the body.

The possibility that viruses may be responsible for the development of carcinoma in man needs further investigation. Experiments on lower animals suggest wide-spread latent infections with carcinogenic viruses. Mider, however, holds that there is no evidence for the viral causation of cancer in man.

The immediate cause of cancer is the production of a self-propagating heritable abnormality in one or more cells. Most carcinogenic agents require a long time to produce such a change. There has been much argument about the nature of this change, including the possibility of some fundamental difference in nuclear constituents. A somatic-mutation theory of cancer has been put forward for the explanation of self-perpetuating changes in somatic cells. Other lines of investigation that may yield profitable results in elucidating carcinogenesis are briefly indicated in the review; for instance the demonstration that certain carcinogens bind tightly with the proteins of the tissues to which they are applied, while yet the neoplasms produced by the agents contain no protein that is capable of binding them.

Chemical properties of cancer cells have been sought that will distinguish them from their normal prototypes, but so far these have been of quantitative rather than qualitative nature. New techniques will need to be devised to measure small quantities of known entities for the discovery of new reactions and new biochemical compounds. The cancer cell is foreign to the body and there is reason to believe that, as in the development of antimicrobial agents, satisfactory results may be achieved in the selective chemical destruction of the invading neoplastic cells.

A number of drugs are being used in the control of neoplastic diseases. Those currently in clinical use are cytotoxic agents, antimetabolites, antibiotics, hormones, and some miscellaneous substances. They seem to produce their effects in different ways, sometimes on the basis of known metabolic or biochemical mechanisms. They are not specific in destroying the malignant cell, and they affect the normal cell of origin in some degree. Better methods need to be devised to determine which compounds will be of value in man; the neoplasms that develop in mice are not necessarily comparable with those which occur in man. The leukaemias have apparently proved most useful in predicting which compounds investigated in the laboratory will be clinically effective. Great advances in the therapy of cancer could be expected if a suitable system of animal kanker, word deur die outeur oorweeg. Hy gee die moontlikheid aan die hand dat longkanker miskien voortgebring word deur stowwe wat deur die longe afgeskei word, maar die liggaam deur kanale, ander as die asemhalingskanale, binnegaan ; daar is baie bewyse dat karsinogeniese verwekkers 'n endjie van waar hulle die liggaam binnegaan, te werk kan gaan.

Die moontlikheid dat virusse verantwoordelik mag wees vir die ontwikkeling van karsinoom by die mens, moet verder ondersoek word. Eksperimente op laer klasse van diere suggereer verspreide latente besmettings met karsinogeniese virusse. Mider egter, meen dat daar geen bewys van die virus veroorsaking van kanker by die mens is nie.

Die onmiddellike oorsaak van kanker is die voortbrenging van 'n erfbare, self-voortplantende abnormaliteit in een of meer selle. Die meeste van die karsinogeniese verwekkers het 'n lang tydperk nodig om so 'n verandering voort te bring. Baie redenasies is al oor die aard van hierdie verandering gevoer, insluitende die moontlikheid van een of ander fundamentele verskil in kernbestanddele. 'n Liggaams-sumatiese teorie van kanker is aan die hand gegee om die self-voortplantende veranderings by liggaamselle te verklaar. Ander navorsingsbeleide wat voordelige resultate ter opheldering van die oorsprong van karsinoom mag oplewer, word kortliks in die hersiening aangestip; byvoorbeeld, die demonstrasie dat sekere karsinogene stewig verbind met die proteïene van die weefsels waarop hulle aangewend word, terwyl die neoplasmas wat deur die verwekkers voortgebring word, tog geen proteïen bevat wat in staat is om hulle te bind nie.

Daar is gesoek na chemiese eienskappe van kankerselle wat hul van hulle normale prototipes sal onderskei, maar tot dusver was hulle van 'n kwantitatiewe eerder as kwalitatiewe aard. Dit sal nodig wees om nuwe tegnieke te ontwikkel om klein hoeveelhede van bekende entiteite te meet vir die ontdekking van nuwe reaksies en nuwe biochemiese samestellings. Wat die kankersel betref, dit is 'n uitheemse sel en daar is rede om te glo dat, soos by die ontwikkeling van antimikrobiese middels, bevredigende resultate verkry mag word by die selektiewe chemiese vernietiging van binnedringende neoplastiese selle.

'n Aantal geneesmiddels word by die beheer van neoplastiese siektes gebruik. Dié wat hedendaags in kliniese gebruik is, is sitotoksiese middels, antimetaboliete, antibiotika, hormone, en sommige gemengde stowwe. Dit skyn of hulle hul uitwerkings op verskillende wyse voortbring, soms op die basis van bekende metaboliese of biochemiese meganismes. Hulle vernietig nie spesifiek die kwaadaardige sel nie, en hulle tas die normale sel van oorsprong tot 'n sekere mate aan. Beter metodes moet beraam word om vas te stel watter verbindings van waarde by die mens sal wees; die neoplasmas wat by muise ontwikkel, is nie noodwendig vergelykbaar met dié wat by die mens aangetref word nie. Die leukemieë het waarskynlik bewys dat hulle baie nuttig is by die voorspelling vai watter samestellings, wat deur die laboratorium ondersoek word, klinies effektief sal wees. Aansienlike vooruitgang in die terapie van kanker kan verwag word as 'n geskikte stelsel om diere te toets, beskikbaar word.

tests became available. Until such time as potent anti-cancer agents are discovered careful study of the available drugs is essential. Much will be gained in learning how to use them and their congeners more effectively.

1. Mider, G. B. (1956): J. Chron. Dis., **4**, 296.

Tot tyd en wyl kragtige antikanker middels ontdek word, is 'n sorgvuldige bestudering van die beskikbare geneesmiddels noodsaaklik. Veel sal bereik word deur te leer hoe om hulle en hul soortgenote meer effektief te gebruik.

1. Mider, G.B. (1956): Chron. Dis., **4**, 296.

GASTRECTOMY FOR PERFORATED ULCER

In an article by Mr. B. Sender[1] published in this issue (p. 7) immediate gastrectomy is recommended as the treatment of choice in certain cases of perforated peptic ulcer. The cases to which this recommendation applies are those of perforation of an ulcer of chronic type, and more particularly of chronic gastric ulcer, in which a proportion of the cases have been found by different surgeons to be of a carcinomatous nature. Prof. J. H. Louw,[1] of Cape Town, has stated from an extensive experience that 12% of his cases of gastric perforation are malignant, and R. Doll[2] has reported a similar incidence of malignancy in perforated gastric ulcers. Other surgeons report a smaller incidence (De-Bakey[1,3]).

J. M. Emmett[1,4] has stated from his experience that the technical difficulty and risk of gastrectomy performed as an emergency operation is no greater than that of gastrectomy performed as an elective procedure, and Professor Louw holds the same opinion.

The results of simple suture of the perforated ulcer are less favourable with chronic peptic ulcers than with acute ulcers (Taylor *et al.*[1,5] and Gilmour [1,6]) and with gastric perforations than with duodenal (Kirkman[1,7]). In perforated chronic ulcer, then, especially gastric ulcer, there is a case for gastrectomy, whether performed in the emergency of perforation instead of simple suture, or as a second operation after the patient's recovery from the emergency operation of simple suture.

This is the issue raised—whether, in the surgical treatment of perforation of chronic peptic ulcer, an immediate gastrectomy should be performed as the emergency operation, or whether the immediate operation of choice is simple suturing of the perforation, to be followed after some months by gastrectomy. Mr. Sender submits definite indications for the former procedure.

In the consideration of this issue the first point that arises is that the alternative of immediate gastrectomy is only justifiable if it is to be performed by a skilled gastrectomist and under first-class conditions, with an able anaesthetist available with all the medical accessories for modern anaesthetics, adequate illumination, and expert assistance and good after-care. These conditions are found in South Africa only in certain of the largest medical centres; and in their absence the safest line should be taken following Moynihan's dictum 'quick in and quicker out', and the emergency operation limited to simple suture. The additional risk of a second operation 3 months later is not great and the patient's interests in these circumstances will be best served by limiting the emergency operation to a minimum.

Mr. Sender makes it clear that his recommendation of immediate gastrectomy for perforated ulcer does not (apart from certain complications) extend to acute peptic ulcers, in which the results of simple suture are more favourable than in the chronic,[7,6] and that the case for immediate gastrectomy is strongest in perforation of chronic gastric ulcers.

1. Sender, B. (1957): S. Afr. Med. J., **31**, 7.
2. Doll, R. (1950): Brit. Med. J., **1**, 215.
3. De-Bakey, M. E. (1953): Ann. Surg., **138**, 327.
4. Emmett, J. M. *et al.* (1953): *Ibid.*, **138**, 320.
5. Taylor, H. *et al.* (1956): Lancet, **1**, 397.
6. Gilmour, J. (1953): *Ibid.*, **1**, 870.
7. Kirkman, N. F. (1955): Postgrad. Med. J., **31**, 67.

VACCINATION IN PREGNANCY

When, in December 1955, people living in Cape Town were urged to seek vaccination as a precaution against smallpox infection on account of the occurrence of an outbreak of that disease, many enquiries were made of general practitioners and obstetricians whether it was advisable for pregnant women to be vaccinated.

It is well established that, especially in the early months of pregnancy, an attack of rubella on the part of the mother may lead to defects in the child such as cataract, deafness, cardiac defects (e.g. patent ductus and septal defects), microcephaly, mental deficiency, and other abnormalities. It may also result in abortion or miscarriage and neonatal mortality. Other viral diseases in the pregnant mother may have a similar unfortunate result in the foetus, though generally in a smaller proportion of cases than with german measles. Amongst the diseases incriminated are measles, chickenpox and mumps, for example.

Vaccinia is one of the viral diseases, and it is therefore natural that apprehension should be felt about possible maldevelopment of the foetus in the event of vaccinia developing in the expectant mother, and hesitation to extend vaccination to pregnant women. Most investigations into the subject have gone to show that vaccination of the mother does not affect the foetus adversely or increase the risk of abortions, stillbirths, congenital malformations or infant mortality. MacArthur, however, in 1952, investigated a series of vaccinated pregnant women and reported an excessive incidence of defects in

the foetus in cases where the mother had been successfully vaccinated between the 4th and 12th weeks of gestation.

Dr. L. J. Abrahamowitz took advantage of the opportinity afforded by the vaccination campaign in Cape Town to investigate the incidence of stillbirths, neonatal deaths and congenital abnormalities amongst the children of women who had been vaccinated during the first 20 weeks of pregnancy, and to compare it with the incidence in the children of women who had not been vaccinated. An article by Dr. Abrahamowitz on the subject is published in this issue (page 000), the results of which are in accordance with the findings of the workers who have detected no increase in these conditions amongst the children of mothers vaccinated during pregnancy, and do not, therefore, confirm MacArthur's findings.

The weight of evidence is against the withholding from pregnant women of vaccination against smallpox when circumstances make it desirable for them in their own interest or that of the community, to acquire immunity against smallpox.

CURRENT TRENDS IN THE TREATMENT OF PERFORATED PEPTIC ULCER

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Until fairly recently the treatment of perforated peptic ulcer hardly merited discussion, since almost invariably the patient underwent an operation, and just as invariably, this involved simple suture of the ulcer. With the introduction of the antibiotics, improvements in anaesthesia, and better understanding of the patients' fluid and electrolyte requirements, the mortality has steadily declined. In recent years interest has been stimulated in 2 directions. On the one hand a more conservative approach has been advocated, and at the other extreme more radical surgery is being encouraged.

A perforated ulcer may be treated in 3 possible ways: (1) conservatively, (2) by simple suture of the ulcer, or (3) by primary gastrectomy. It is the purpose of this article to discuss the indications for the different proceedures in the light of current trends.

Gilmour,[1] in 1953, was the first to draw attention to the significant difference in mortality and morbidity between perforated acute and perforated chronic ulcer. The differences between acute and chronic ulcers may be summarized thus:

1. In the acute ulcer a history of dyspepsia is either entirely absent or has not been present for longer than 3 months, whereas in perforated chronic ulcers a story is usually obtained of recurrent bouts of painful dyspepsia.

2. At operation the stomach or duodenal wall, in acute perforations, is perfectly mobile and somewhat hyperaemic, and the perforation is punched out and generally small. In chronic ulcers the perforation is usually larger than in the acute cases, and the state of the wall gives evidence of a long-standing pathological process. It is stiff and unyielding and feels fibrotic, and scarring and deformity is usually a marked feature.

By a consideration of the history of the case before perforation, and of the operative findings, Gilmour is of the opinion that the type of ulcer can be diagnosed with confidence in nearly all cases. It is of great interest to note that neither Gilmour (in 119 cases) nor Taylor[2] (in 47) had a single fatality in their acute perforations. This must be contrasted with their 14% mortality for chronic ulcers (Taylor) and 15% (Gilmour). Taylor treated his cases by conservative measures, which will be discussed later, and Gilmour treated all of his by simple suture. When the reasons for this startling difference in mortality between acute and chronic ulcers are considered, it is clear that, in the latter, factors such as chronic ill-health, electrolyte imbalance and protein deficiency assossiated with pyloric stenosis are of first importance. Henley[3] is also of the opinion that the fatal outcome in some cases is the result of failure to secure obliteration of the perforation because of the immobility of the area.

Another fact which emerges from the recent literature, is the constantly worse prognosis in gastric perforations as opposed to duodenal perforations. Kirkman[4] records a 12% mortality for gastric perforations treated by suture, and contrasts this with his 2·5% mortality for duodenal cases. Many writers have reported similar findings. The perforated duodenal ulcer shows a much greater tendency than the perforated gastric ulcer to become either partially or completely sealed off by a neighbouring viscus or omentum and, for that reason, peritoneal soiling is often surprisingly small in amount in duodenal perforations.

Perforation of a gastric carcinoma is commoner than was previously thought. Aird, in 1935, could only find 71 cases in the literature, but since then large series have been reported. It is important to realize that perforated carcinoma does not result in the early development of peritoneal secondaries (Doll[5]). It may, indeed, occur when the lesion is very localized, and in the absence of gland or hepatic involvement. My own recent experience may be mentioned in this connection. Immediate gastrectomy has been performed in 7 of the last 13 perforations operated on. There was no mortality in the patients who underwent resection. In the remaining 6 cases there was 1 death from a catastrophic haemorrhage on the 10th day after simple suture of a duodenal ulcer. This is a very small personal series, from which it is not proposed, and niether is it possible, to draw any conclusions. There is, however, some significance in the fact that of the 7 primary gastrectomies (5 for gastric perforations and 2 for duodenal) 2 were shown on sub-

sequent histology to be carcinomatous. In neither case was there peritoneal, glandular or hepatic involvement. Oddly enough these were successive cases admitted within weeks of each other to the same ward of Groote Schuur hospital. Prof. J. H. Louw[6] has stated from his extensive experience of gastric surgery that 12% of gastric perforations are malignant. Bisgaard[7] reviewed 217 cases of perforated gastric carcinoma and found that the pre-operative diagnosis was made in only 7. He remarks on the great number of cases thought by the surgeon to be benign, and emphasizes the smallness and well localized appearance of the carcinoma at the time of rupture.

It is apparent, then, that there can be no one form of treatment suitable for all cases of perforated ulcer.

CONSERVATIVE TREATMENT

Taylor has probably been the most enthusiastic supporter of this form of management, first used by Wangensteen. The stomach is kept empty by suction through a Ryle's tube, fluids and electrolytes are replaced, and this is combined with sedation and appropriate antibiotic cover. The amount of gas under the diaphragm is noted, and another X ray is taken 12 hours later. If the second picture reveals an increase in the amount of gas, operation is considered. Surgical measures are invoked only to deal with a residual collection of fluid in the abdomen, should this occur. The conservative method of treatment demands constant vigilance by a nursing staff well drilled in the method. Taylor reported on a series of 200 cases treated in this manner over a period of 10 years. As stated above, he had no deaths in his 47 cases of acute perforation, and a 14% fatality in chronic ulcers. In the absence of surgical exposure he differentiates acute ulcers from chronic on the basis of the history alone. While it is true that an acute ulcer very rarely gives a definite history of dyspepsia, and certainly not a painful dyspepsia, it is well known that an obviously chronic ulcer, as judged by its operative appearance, may occasionally exist with minimal symptoms and then perforate. Fig. 1 shows a chronic perforated ulcer in a man of 41, who denied having had dyspepsia of any sort prior to perforation. Taylor is firmly of the opinion that if an acute ulcer is treated conservatively the patient will survive and experience no further trouble from his ulcer. Only 3 of his 47 cases so treated developed dyspepsia over the next 10 years. On the other hand 25% of Gilmour's patients treated by simple suture developed chronic ulcers in the next 7 years. Taylor feels that the reason for this lies in the fact that the suturing of an acute ulcer distorts the wall of the stomach or duodenum, introduces foreign bodies, and interferes with the local blood supply, the nett result being a vulnerable scar predisposing to chronic ulceration. This is a view which is not easy to accept. It is of interest to note that Nuboer[8] has gone on record with the statement that a peptic ulcer which has perforated is not acute but must, in the nature of the lesion, be a chronic pathological process. He has examined a large number of so-called acute perforations histologically and finds that they all satisfy the criteria of chronicity. If his views are correct it follows that a very high percentage of chronic ulcers evince no significant symptoms of dyspepsia.

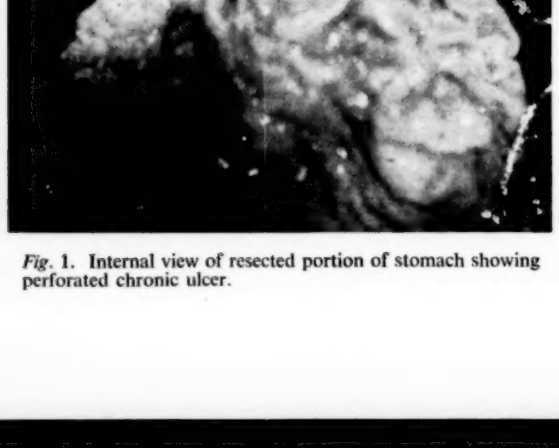

Fig. 1. Internal view of resected portion of stomach showing perforated chronic ulcer.

Taylor's work is important in that it emphasizes that a patient with a perforated ulcer does not of necessity require an immediate operation; where there are medical contra-indications to operation this is a comforting thing to know. There are, however, several disadvantages connected with the universal adoption of this form of therapy. Errors in diagnosis may have serious consequences, and Taylor himself has pointed out that this may occur in 2 directions: (1) Other acute conditions may be diagnosed as perforated ulcer, and (2) perforations may be diagnosed as some other abdominal emergency. The risk also exists that the perforation may be carcinomatous.

Under the first heading, Taylor had 2 cases of appendicitis and 2 cases of intestinal strangulation treated at the start by aspiration, and later by operation, when the true diagnosis became apparent. In 4 other cases aspiration treatment was continued when the correct diagnosis was eventually made; of these, 2 were cases of biliary colic, 1 of gastro-enteritis, and 1 of coronary thrombosis.

Under the second heading there were 9 mistaken diagnoses—7 cases of acute appendicitis, and 1 each of intestinal obstruction and perforated diverticulitis, in patients in whom there actually was a perforated peptic ulcer.

Beattie[9] treated 40 cases conservatively, as an experiment. Of these, 32 were cases of duodenal ulcer, of which 1 died; and 7 of gastric ulcers, of which 4 died. The remaining one was a case of a carcinoma, in whom death also occurred. As a result of these unsatisfactory figures, Beattie has reverted to early laparotomy.

It would appear that conservative treatment has a definite place in the treatment of perforated ulcer, but that its use should usually be limited to perforations occurring in patients where operation is contra-indicated for medical reasons.

It is not yet certain whether the moribund patient does better on conservative or on operative treatment. Dendy Moore[10] is strongly of the opinion that such patients will all die if treated by aspiration, but that some will recover if the peritoneum is cleared of fluid at operation and vigorous resuscitation applied.

OPERATIVE TREATMENT

Simple suture is still the most popular operation for perforated ulcer. There has been a steady decline in mortality, well illustrated by the figures of Avery Jones.[11] In the period 1938-40 he reported 27 deaths in 106 cases. From 1947 to 1948 he had 4 deaths in the same number of cases. He comments also on the changing factors responsible for death. Before 1943, which is about the time when the antibiotics were introduced, the patient died early from the effects of shock and general peritonitis. Today death tends to occur later, from haemorrhage, subphrenic or pelvic abscess, or other complications, especially pulmonary.

With the increased safety of operations, and improvements in pre-operative and post-operative care, more attention is being paid to the long-term sequelae of simple suture. Matheson,[12] reviewing 115 cases treated by simple suture, found that perforation had recurred in no fewer than 11%, and that 50% of all the cases eventually required further surgery. Turner[13] finds that 85% show a recurrence of symptoms after suture and is of the opinion that all survivors should be submitted to resection in the immediate post-operative period. Henley[3] also finds that only 1 in 5 patients will remain symptom-free after suture.

As stated above, recurrence of symptoms is a complication of perforated chronic ulcer only, and is very rare indeed after perforation of an acute ulcer.

With the realization that the long-term results after suture are unsatisfactory in something like 70% of cases, an increasing number of surgeons are advocating primary gastrectomy as the procedure of choice. Henley reports on 22 primary resections with 2 deaths. During the same period 36 patients underwent simple suture also with 2 deaths. De-Bakey[14] recorded 55 gastrectomies with 1 death. In his series 2 of the gastric ulcers later proved to be carcinomatous. He stated that 75% of the gastrectomies were performed during the first 12 hours after perforation, and 10% as late as 24 hours after perforation. The longer period does not necessarily contraindicate resection. The number of hours that has elapsed since perforation is not always a reliable guide to the patient's ability to withstand a major operation; what is important is the degree of peritoneal contamination and consequent shock. It often happens, especially in duodenal perforations, that partial or complete sealing off of the area by a neighbouring viscus has occurred. In these cases peritoneal contamination is often surprisingly small even 10-12 hours after perforation.

Those who oppose primary gastrectomy as the treatment of choice do so on the ground that the need is to save life and that the quickest and most effective way of doing this is by simple suture. Downie[15] asks: 'Why is it better to stop the leak by an operation lasting 1½ hours on a patient in a rather delicate state of health, when it can be stopped quite easily by an operation lasting 15 minutes?' Critics of the radical operation, done as an emergency, base a large part of their case on the commonly-held idea that mortality following simple suture is significantly less than that following gastrectomy. In fact, as Nuboer has pointed out, the reverse is true.

A good deal of confusion has arisen because many writers tend to assume that surgical opinion is divided into 2 camps, viz. those who would undertake gastrectomy in every case of perforation and those who would perform simple suture in every case. The fact is, of course, that each operation has its part to play, and the problem is to decide which operation, performed at the time of perforation, will give the best results, both immediately and later.

It has been shown that some 30% of patients are symptom-free after simple suture, and most of these belong to the group of acute perforations, in which a good result can nearly always be confidently expected. If the policy were adopted of performing primary gastrectomy in all cases, it would involve unnecessary mutilation in this 30%.

In view of the fact that fully 70% of chronic ulcers will require further surgery after simple suture, there is a very good case for performing primary gastrectomy in these cases. But it is necessary to observe strict criteria in choosing the right type of case for gastrectomy. There should be a history of painful dyspepsia of at least 18 months, and at operation the ulcer should possess the features of chronicity as described above. Each case must be considered individually. In some cases the indications for resection exist, but the operation is not feasible at the time by virtue of the patient's condition. In these cases it is probably a reasonable procedure to perform gastrectomy in the 3 months period following perforation. Many surgeons favour the routine performance of gastrectomy after recovery from suture. However, if a patient is able to stand gastrectomy at the time of the emergency, it does not seem reasonable to subject him to 2 operations.

In contemplating gastrectomy for perforations of duodenal ulcers the difficulty sometimes experienced in invaginating an inflamed and oedematous duodenum should be borne in mind in making an early assessment of the feasibility of resection. Emmett[16] has stated that the techincal difficulty of the gastrectomy performed as an emergency operation is no greater than that performed as an elective procedure. He had to date performed 46 resections with no mortality. Prof. J. H. Louw[17] supports this opinion. He has found all his gastrectomies for perforation to be 'on the easy side' technically, and his cases have all done very well; indeed, better than the cases of simple suture, and as well as elective gastrectomies. It is important to stress these points because the idea seems to be current that immediate gastrectomy in these cases is a hazardous affair, with a stormy post-operative course to be expected.

Emmett found that 2 of his first 7 primary gastrectomies were shown on histology to be carcinomatous. One of the two remained well after 6 years, thus illustrating the point that perforation of a gastric carcinoma does not always herald immediate spread.

As regards gastric perforation, there can be few today who would deny that gastrectomy, where feasible, is the correct procedure for this condition. The high mortality following simple suture in this site, and the 12% chance that the ulcer is malignant, dictate such an attitude.

Biopsy of a perforated gastric ulcer, to exclude malignancy, followed by simple suture, is usually not a satisfactory procedure. The surgeon, in his anxiety to secure a good closure, may be tempted to take an inadequate snip, and a negative biopsy under these circumstances may well be a death warrant.

I submit the following as a fair assessment of the present position:

Indications for Conservative Treatment

1. Patients who for medical reasons are unable to undergo operation
2. Moribund patients

Indications for Simple Suture

1. Acute perforations
2. Chronic duodenal perforations with a history of less than 1 year.
3. Cases where gastrectomy is indicated but the condition of the patient precludes it.
4. Moribund patients—perhaps limited to peritoneal drainage.

Indications for Primary Gastrectomy

1. Bleeding perforated ulcers
2. Perforated carcinomas
3. Gastric ulcers
4. Perforations associated with pyloric stenosis
5. Recurrent perforations.

SUMMARY

1. This survey indicates that primary gastrectomy for perforated ulcer has a fairly well defined place in treatment.

2. The difference in prognosis between acute and chronic perforations, stressed in the recent literature, is commented on.

3. The very real risk is emphasized that a perforated gastric ulcer may be malignant.

4. The relative place in treatment of conservative measures and the different operative forms of treatment is discussed.

I wish to thank Prof. J. H. Louw, Head of the Department of Surgery, University of Cape Town, for his kind advice and encouragement. I am grateful also to Mr. George Sacks for permission to operate on cases mentioned, who were admitted to his beds at the Groote Schuur Hospital, Cape Town, and to Mr. L. Chanock and Mr. M. Margo for the same privilege in relation to patients admitted to their beds at the Somerset Hospital, Cape Town.

REFERENCES

1. Gilmour, J. (1953): Lancet, **1**, 870.
2. Taylor, H. and Warren, R. P. (1956): *Ibid.*, **1**, 397.
3. Henley, A. (1955): Postgrad. Med. J., **31**, 242.
4. Kirkman, N. F. (1955): *Ibid.*, **31**, 67.
5. Doll, R. (1950): Brit. Med. J., **1**, 215.
6. Louw, J. H. (1956): Lecture, Groote Schuur Hospital, Cape Town.
7. Bisgaard, J. D. *et al.* (1945): Surgery, **17**, 498.
8. Nuboer, J. F. (1951): Lancet, **2**, 952.
9. Beattie, A. D. Quoted by Edwards, H. (1954): *Recent Advances in Surgery*, 4th ed. London: Churchill.
10. Moore, H. D. (1956): Lancet, **1**, 579.
11. Jones, F. A. *et al.* (1950): Brit. Med. J., **1**, 211.
12. Matheson, T. (1956): Brit. J. Surg., **43**, 641.
13. Turner, F. P. (1951): Surg. Gynec. Obstet., **92**, 281.
14. De-Bakey, M. E. (1953): Ann. Surg., **138**, 327.
15. Downie, V. J. (1956): Lancet, **1**, 952.
16. Emmett, J. M. *et al.* (1953): Ann. Surg., **138**, 320.
17. Louw, J. H. (1956): Personal communication.

MEGALOBLASTIC ANAEMIA OF PREGNANCY

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Walter Channing,[1] in 1842, was the first to distinguish an anaemia occurring during pregnancy and the puerperium and not due to loss of blood. This disease has for many years been known as pernicious anaemia of pregnancy and the puerperium. In 1919, Sir William Osler[2] drew attention to the fact that the disease differed from Addisonian pernicious anaemia in that, when it took place, recovery was permanent, although recurrence in a subsequent pregnancy was liable to occur. Only in 1942[3] was the term 'megaloblastic anaemia of pregnancy' proposed as a substitute for the name 'pernicious anaemia of pregnancy.'

Since the recognition of this disease there have been many surveys reported in the literature. It is noticeable that very few cases have been diagnosed during the antenatal period.

In a survey of the past 20 years Scott,[4] in 1954, collected 114 cases occurring in the United Kingdom, of which only 20 had been treated during their pregnancy. She reports a further 37 cases, of which 19 were treated before the onset of labour.

In Davidson, Davis and Innes' series of 16 cases[3] only 2 were treated antenatally.

Stevenson[5] saw 5 of her 38 cases before delivery. Only 2 of the 6 infants born at these 5 confinements survived and one mother died 4 days after the confinement. All the infants except one were born prematurely.

In a large series of 45 patients reported by Thompson and Ungley[6] only 7 cases were diagnosed before labour commenced.

Patel and Kocher[7] report 5 cases of macrocytic anaemia of pregnancy and the puerperium of which 4 were diagnosed before the onset of labour. Whether all these cases were pure megaloblastic anaemias of pregnancy is doubtful. A nutritional bases is suggested by the fact that 2 of the patients were refugees and the

3rd was in a very poor economic state. The same doubt is cast on the 5 cases reported by Chaudhuri.[8]

In South Africa Cohen[9] records 5 cases occurring in pure Bantu women, all diagnosed *post partum*. Adams and Wilmot[10] report 14 cases, 6 African and 8 Indian, of which only one was seen before delivery, in the 38th week of her pregnancy.

Seven cases of megaloblastic anaemia of pregnancy have been diagnosed at the Queen Victoria Maternity Hospital, Johannesburg, all diagnosed and treated during the antenatal period, and all of European descent. They all claimed to have consumed a good daily diet, which included meat at least 3 times a week.

Incidence

The true incidence of pernicious anaemia of pregnancy and the puerperium is difficult to estimate, but it must certainly be considerably higher than the literature suggests. The present cases were all diagnosed at the Queen Victoria Maternity Hospital in a period of 18 months (from March 1955 to August 1956) during which 7,500 cases were attended to at the antenatal clinic.

Evans[11] found no cases in 4,000 pregnancies, Boycott[12] none in 222 and Reid and Mackintosh[13] none in 1,108.

Stevenson[5] reported 100 cases of anaemia in pregnancy and the puerperium, of which 30 were of the megaloblastic type. Davidson, Davis and Innes[3] saw 16 cases in 2 years, during which period there were 8,000 confinements in the hospitals concerned. Davidson, Girdwood and Clark[14] in 7 years collected 521 cases of macrocytic anaemia, yet only 31 cases were associated with pregnancy. Thompson and Ungley[6] reviewed 45 cases which had been collected over a period of 17 years.

Age

The mean age seems to be commonly in the early part of the 4th decade of life, as shown in the following series:

Series	*Mean Age*
Davidson, Davis and Innes[3] (1942)	30·8 years.
Miller and Studdert[17] (1942)	31 ,,
Thompson and Ungley[6] (1951)	31 ,,
Clark[16] (1952)	33 ,,
Present series (1956)	28·7 ,,

These figures are in contrast to those seen in Addisonian pernicious anaemia, where the greatest incidence occurs between the ages of 40 to 70 years.[15]

Previous Pregnancies

The condition is more commonly seen in women who have had previous pregnancies, especially if these have followed each other in rapid succession.[16,6,17,5]

All the cases except one in the present series were multiparae, as shown in the following table:

Case No.	*Pregnancies*	*Frequency*
1	10	1942, 44*, 45*, 46, 48, 50, 51*, 52*, 53*, 55
2	3	1953, 54, 55
3	9	1943, 45, 46, 48, 50, 52, 53, 55*, 56
4	6	1948, 49, 50, 52, 54, 56
5	6	1943, 44, 47, 51, 55*, 56.
6	1	1956
7	2	1951, 56

* Abortions.

Megaloblastic anaemia is diagnosed more often in multiparae because it is in these cases that the anaemia is most likely to be severe, giving rise to symptoms which require investigation. That the condition is less common in primigravidae is difficult to believe, although it may be less severe in primigravidae and in those who have borne few children. Case 6 might be cited as an example. She had a relatively mild anaemia, which could easily have been overlooked during her pregnancy and puerperium. With frequent subsequent pregnancies the anaemia, untreated, is not allowed to recover and becomes aggravated with each pregnancy until eventually the diagnosis is obvious. By this time the patient is classified as a grande multipara.

Gastric Analysis

In Addisonian pernicious anaemia achylia is always a feature.[18]

The incidence of histamine-fast achlorhydria in cases of megaloblastic anaemia of pregnancy varies in different series, as follows:

	Free HCl	*Hypochlorhydria*	*Achlorhydria*
Clark[16]	10	—	6
Patel and Kocher[7]	5	—	1
Miller and Studdert[17]	—	7	3
Badendoch *et al.*[19]	7	—	2
Present series	1	2	3

CASE REPORTS

Case 1

Mrs. K.P., age 31 years, gravida 10, para 4. This patient was first seen at the antenatal clinic on 10 March 1955, when she was approximately 26 weeks pregnant. She had had 4 full-term normal pregnancies and 3 abortions at 4 weeks (see table on page 0000). During 1951 a pregnancy ended at 7 months with a stillbirth. Following on the abortion in 1953 a currettage was performed and a blood transfusion was administered.

In a routine estimation made at the clinic the haemoglobin was found to be 8·8 g.%. Her blood group was A and she was Rh=positive.

The patient was treated with oral ferrous sulphate, 6 gr. thrice daily, and only returned to the clinic on 2 May. The haemoglobin was then found to be 9·3 g.%, and she was admitted to hospital for investigation.

On admission general examination revealed a few carious teeth but no glossitis. The blood pressure was 104/60 mm. Hg, and no abnormal physical signs were detected. She was approximately 33 weeks pregnant.

Blood examination at this stage revealed a haemoglobin of 9·3 g.%, packed cell volume 33%, mean corpuscular volume 94 c. microns. Mean corpuscular haemoglobin concentration 28%, leucocytes 12,300 per c.mm. The red cells showed marked anisopoikilocytosis and some cells were markedly macrocytic and normochromic in appearance. The direct Coombs test was negative.

A gastric analysis revealed a histamine-fast achlorhydria, and this was confirmed on repeating the test 2 days later. Tests for blood and parasites in the stools were negative.

Owing to domestic difficulties the patient did not remain in hospital so that a sternal marrow could not then be done, but she returned to the clinic on 2 June and consented to be admitted for sternal marrow examination. The haemoglobin was now 8·3 g.%, the erythrocyte count 2·96 millions per c.mm., and the leucocyte count 10,600 per c.mm.

The sternal marrow examination confirmed the diagnosis of a megaloblastic anaemia. The patient was now approximately 36 weeks pregnant. A precordial systolic cardiac murmur could be heard.

The patient was therefore given a transfusion of 500 c.c. whole blood and this procedure was repeated 2 days later. Therapy with vitamin B 12, 150 micrograms intramuscularly thrice weekly, was instituted on 9 June.

One day before delivery a further gastric analysis showed the presence of a small amount of free hydrochloric acid, but only in response to histamine injection.

Normal delivery of a female child weighing 5 lb. 10 oz. took place on 25 June. The third stage of labour was complicated by the loss of 40 oz. of blood, and a further 500 c.c. of whole blood was administered.

The patient was discharged on the 10th postpartum day, after an uneventful puerperium, the haemoglobin being 11·5 g.%. The results of blood examinations in this case were as follows:

Date	*Hb. g.%*	*RBC millions per c.mm.*	*Reticulocytes %*	*MCV c. microns*	*PCV %*	*MCHC %*
2 May	9·3	—	3·5	94	33	28
16 May	10·0	—	—	—	29	35
26 May	9·3	3·55	2·9	86	30·5	30·5
2 June	8·3	2·96	—	—	—	—
6 June	10·3	—	2	—	35	30
9 June	12·2	—	1	—	—	—
13 June	—	—	2	—	—	—
17 June	11·7	—	2·8	—	37	32
24 June	12·0	—	1·1	—	—	—
5 July	11·5	—	—	—	—	—

Case 2

Mrs. P.D., age 24 years, para 2, gravida 3. This patient attended antenatal clinic for the first time on 12 August 1955, when she was 22 weeks pregnant. She had had 2 previous normal pregnancies, in 1953 and 1954. Both deliveries and postpartum periods were normal.

By a routine estimation made at this visit the haemoglobin was found to be 10·3 g.%. Her blood group was A, and she was Rh—positive.

Six days later the patient was admitted to hospital with the diagnosis of a threatened abortion. She responded to treatment and was discharged after 4 days.

One month later (28 October) she was readmitted to hospital for the investigation of an anaemia. Her haemoglobin was then 9·8 g.%.

On admission she said that she felt well and had no symptoms at all.

She looked very pale and on examination was found to be approximately 33 weeks pregnant. The blood pressure was 120/60 mm. Hg. There was no glossitis present. The remainder of the physical examination revealed no abnormality.

A blood count at this time was as follows: Haemoglobin 8·9 g.%, erythrocytes 3·6 millions per c.mm., leucocytes 6,100 per c.mm., mean corpuscular volume 75 c. microns, mean corpuscular haemoglobin concentration 33%. The red cells were normochromic and showed moderate anisopoikilocytosis; macrocytes were observed in the peripheral blood on 31 October. The platelets appeared normal.

While the report on the blood was awaited the patient started labour prematurely. She was heavily sedated with calcium phenobarbitone, and in view of the anaemia transfused with 500 c.c. of whole blood (29 October). The uterine contractions subsided and on 1 November a sternal marrow examination was made, which confirmed the diagnosis of megaloblastic anaemia.

The direct Cooms test was negative. Gastric analysis showed abundant free hydrochloric acid to be present. Serum iron 652 micrograms per 100 ml. Serum bilirubin less than 0·5 mg. per 100 ml.

Folic acid therapy was commenced on 2 November—10 mg. orally thrice daily. Treatment continued as an out-patient and the patient was readmitted to hospital 6 days before delivery.

Labour lasting 14½ hours, commenced on 15 December, and a normal male child weighing 8 lb. 10 oz. was delivered. The blood loss was 22 oz.

The puerperium was uneventful and the patient was discharged from hospital on the 10th postpartum day with a haemoglobin of 13·5 g.%. The results of blood examinations in this case were as follows:

Date	*Hb. g.%*	*RBC millions per c.mm.*	*PCV %*	*MCV c. microns*	*MCHC %*	*Reticulocytes %*
28 October	8·9	3·6	27	75	33	—
31 October	10·6	3·96	32·5	81	33	2·5
4 November	10·6	3·9	32·5	84	33	4·0
7 November	11·3	—	—	—	—	3·0
9 November	11·0	—	36	—	31	1·5
18 November	12·9	4·6	39	85	33	0·5
25 November	11·8	—	37	—	32	1·0
30 November	12·8	4·4	—	—	—	0·5
12 December	12·5	4·25	38·5	89	33	0·5
20 December	12·3	4·2	37	88	33	1·5
24 December	13·5	4·61	40·5	88	33	1·0

Case 3

Mrs. M.F., aged 30 years, para 7, gravida 9. This patient attended the antenatal clinic for the first time on 7 March 1956. Because of albuminuria she was admitted to hospital for investigation. There was some uncertainty about the date of her last menstrual period but calculating from the date of quickening she was thought to be 36-38 weeks pregnant. The first 7 pregnancies were all full term and normal. The 8th pregnancy aborted at 12 weeks (see table on page 0000).

The only symptoms of which the patient complained was a severe intermittent headache which had troubled her during the pregnancy.

With the exception of a marked pallor there were no abnormal physical signs. Abdominal palpation revealed a pregnancy of 36-38 weeks duration. A catheter specimen of urine contained a trace of albumen and on microscopic examination nothing of significance was detected.

A blood count made on admission gave the following results: Haemoglobin 8·0 g.%, erythrocytes 3·0 millions per c.mm., packed cell volume 25%, mean corpuscular volume 84 c. microns, mean corpuscular haemoglobin concentration 32%, leucocytes 8,000 per c.mm. Diffuse basophilia, macrocytosis, poikilocytosis, anisocytosis and normochromia were present. The blood group was O, and the patient was Rh—negative.

A sternal marrow examination confirmed the diagnosis of

megaloblastic anaemia. Unfortunately a gastric analysis was not done.

Treatment with folic acid, 10 mg. orally thrice daily, was commenced on 13 March, and because of the advanced stage of her pregnancy the patient was also given a blood transfusion of packed cells from 1,000 c.c. of whole blood.

Labour began spontaneously and unexpectedly the following day (i.e. 6 days after admission). The labour lasted only 6 hours and a live healthy male child weighing 6 lb. 2 oz. was born. The third stage of labour was complicated by the loss of 55 oz. of blood, and a further transfusion of 1,000 c.c. whole blood was given.

The puerperium was uneventful and the patient was discharged on the 11th postpartum day, when the haemoglobin was 13 g.%. The results of haemoglobin and reticulocyte examinations were as follows:

Date	8/3	14/3	15/3	16/3	17/3	18/3	19/3	20/3	21/3	22/3	23/3
Hb. g.%	8	9·8	11	10·8	11·6	—	—	13·0	13·0	—	13
Reticulocytes%	—	3·5	1·5	3·0	2·0	1·0	1·0	1·0	0·6	1·0	—

Case 4

Mrs. A.G., age 28 years, para 5, gravida 6. This patient first attended the antenatal clinic on 9 February 1956 and was then about 33 weeks pregnant, the expected date of delivery being on 1 April.

A blood investigation made at the clinic on 13 March revealed haemoglobin 6·2 g.%, erythrocytes 2·5 millions per c.mm., and leucocytes 4,500 per c.mm. There was diffuse basophilia, poikilocytosis, anisocytosis and hypochromia. The platelets appeared normal. The blood grouping was O and the patient was Rh− positive.

On 21 March she was admitted to hospital for investigation. She had had 5 full-term normal pregnancies, 2 of which were complicated by postpartum haemorrhage. The first pregnancy was in 1948 and the last in 1954. On questioning she complained only of feeling weak.

The patient looked pale, with a slight lemon yellow tinge of the skin. The blood pressure was 130/60 mm. Hg, the heart rate 100 per minute. A soft systolic murmur was heard at the apex. No hepatosplenomegaly or lymphadenopathy were observed. There was no glossitis and the patient was apyrexial. She was then about 38 weeks pregnant.

A blood count on admission gave the following results: Haemoglobin 7·6 g.%, erythrocytes 2·8 millions per c.mm., haematocrit 24·5%, mean corpuscular volume 87·0 c. microns, mean corpuscular haemoglobin concentration 31%, leucocytes 10,800 per c.mm. Diffuse basophilia and macrocytosis was present. The serum bilirubin was less than 0·5 mg. per 100 ml. Serum proteins 5·2 g. per 100 ml. (Albumin 2·6, globulin 2·6).

A bone-marrow examination was made and this confirmed the diagnosis of megaloblastic anaemia. Gastric analysis revealed a histamine-fast achlorhydria.

In view of the advanced state of the pregnancy the patient was given a slow transfusion of packed cells from 1,000 c.c. of whole blood on 22 March, and oral therapy of folic acid, 10 mg. thrice daily, was commenced.

Spontaneous labour started on 3 April, and after a normal labour lasting 11½ hours the patient was delivered of a healthy male child weighing 6 lb. 8 oz. The blood loss was 14 oz.

The puerperium was uneventful and the patient was discharged on the 10th postpartum day with a haemoglobin of 13 g.%. The results of haemoglobin and reticulocyte examinations were as follows:

Date	13/3	21/3	22/3	24/3	26/3	27/3	28/3	29/3	31/3	3/4	5/4	9/4	13/4
Hb. g.%	6·2	7·6	—	10	10·9	12·5	—	12·4	11·0	12·2	12	12	13·0
Reticulocytes %	—	—	1·5	2·0	2·0	3	2·6	4·0	3·0	3·5	—	2	—

Case 5

Mrs. J.v.N., age 32 years, para 4, gravida 6. This patient was admitted to hospital on 29 April 1956 because of a haemoglobin of 9·1 g.% found during routine examination at the antenatal clinic. The erythrocyte count was 3·93 millions per c.mm., haematocrit 28%, mean corpuscular volume 87 c. microns, mean corpuscular haemoglobin concentration 32·5%. The red cells showed normochromia, anisocytosis and macrocytosis. White-cell count 7,200 per c.mm. The blood group was A and the patient was Rh−positive.

She had had 4 full-term normal pregnancies, the first in 1953 and the last in 1956. The last pregnancy, however, was associated with a raised blood-pressure. In June 1955 she aborted at 8 weeks and received a blood transfusion. The expected date of delivery of the present pregnancy was calculated to be 14 June. She had been well throughout her pregnancy.

On admission the blood pressure was 130/90 mm. Hg. No oedema or albuminuria was detected. No abnormality was found on general examination except for some degree of pallor. She was approximately 33 weeks pregnant.

A sternal marrow examination confirmed the diagnosis of megaloblastic anaemia. Gastric analysis revealed a histamine-fast achlorhydria.

Folic acid, 15 mg. orally thrice daily, was commenced on 30 April. A transfusion of packed cells from 1,000 c.c. of whole blood was given on 11 May.

The patient was discharged from hospital on 25 May with a haemoglobin of 13·9 g.% and a normal peripheral blood picture, and was kept on a maintenance dose of folic acid.

One week later she was readmitted to hospital with a raised blood-pressure and slight oedema of the legs. She responded to sedative therapy and remained in hospital for only 4 days.

Five days later she was again readmitted to hospital with a blood pressure of 150/90 mm. Hg. No albuminuria was present. There was slight oedema of both legs.

During this admission the blood pressure did not return to normal and as the pregnancy was at full term a medical induction was started on 16 June. Labour commenced soon after the induction, and when the membranes ruptured the liquor amnii was profusely stained with meconium, which caused some concern. Labour lasted 4½ hours and the patient was delivered of a healthy male infant weighing 7 lb. 6 oz. The blood loss was 6 oz.

Except for a slightly raised blood pressure during the first 3 days, the puerperium was uneventful and the patient was discharged on the 10th postpartum day with a normal blood pressure and blood count. The results of haemoglobin and reticulocyte examinations were as follows:

Date	20/4	30/4	1/5	2/5	3/5	5/5	7/5	8/5	9/5	11/5	12/5	19/5	23/5	15/6
Hb. g.%	9·1	9·4	9·5	—	9·1	9·3	—	—	10·5	10·6	12·7	13·9	14·1	14·1
Reticulocytes %	—	2	2	3·5	—	4	3·6	3·0	2·5	2	1·5	—	—	—

Case 6

Mrs. v.d.L., age 20 years, primigravida. This patient attended the antenatal clinic for the first time on 31 July 1956, when she was 36 weeks pregnant, the expected date of delivery being 27 August. The routine haemoglobin estimation made at this time showed 10·3 g.%. On 13 August she was admitted to hospital for investigation.

On admission she felt well and did not complain of any untoward symptoms.

On examination she looked pale, blood pressure 140/75 mm. Hg, and no hepatosplenomegaly was present and no glossitis. She was then approximately 38 weeks pregnant.

Haematological investigation showed haemoglobin 10 g.%, red-cell count 3·6 millions per c.mm., packed cell volume 33%, mean corpuscular volume 93 c. microns, mean corpuscular haemoglobin concentration 31%, leucocytes 14,500 per c.mm. The red cells showed normochromia, anisocytosis, macrocytosis and diffuse basophilia. The platelets appeared normal and the prothrombin index was 88%.

Two days later a bone-marrow examination was made, which revealed the picture of a megaloblastic anaemia. Gastric analysis performed on 15 August revealed a histamine-fast achlorhydria; this was repeated and confirmed on 23 August.

Bilirubin 0·5 mg.%. Blood urea 14 mg. per 100 c.c. Plasma uric acid 5·5 mg. per 100 ml. Serum iron 137 mg. per 100 ml.

Therapy with folic acid, 10 mg. b.d. orally, was begun on 15 August.

Spontaneous labour began on 3 September and lasted 18 hours. A normal male child weighing 8 lb. was born. The blood loss was 7 oz.

On admission the patient looked pale. There were no other abnormal physical findings. She was approximately 38 weeks pregnant.

A sternal marrow examination made on admission revealed the picture of a megaloblastic anaemia. Gastric analysis showed that there was a small amount of free hydrochloric acid present. There was no response to injections of histamine.

Oral therapy of folic acid, 10 mg. t.d.s., was instituted on 24 August.

Spontaneous labour started on 8 September and after 8 hours a normal healthy male child weighing 8 lb. 12 oz. was born. The blood loss in the third stage was 12 oz.

The puerperium was uneventful. The infant, however, contracted diarrhoea, so that the mother and child were not discharged from hospital until the 15th day. The haemoglobin of the mother on discharge was 13·6 g.%. The results of blood examinations in this case were as follows:

Date	*Hb. g.%*	*RBC millions per c.mm.*	*PCV %*	*MCHC %*	*Reticulocytes %*
29 March	10·8	3·8	—	—	—
22 May	10·6	3·75	—	—	—
23 August	11·0	—	35	31·5	2·8
27 August	10·7	—	32	35	2·6
28 August	10·2	—	—	—	3·8
29 August	10·6	—	33	34	4·8
30 August	10·6	—	34	33	3·6
31 August	11	—	33	33	2·4
1 September	10·7	—	35	31	2·3
4 September	10·6	—	31	34	2·1
5 September	10·5	—	32	33	2·5
6 September	10·3	—	31	33	2·2
7 September	11·8	—	37	32	1·7
8 September	11·2	—	36	31	2·7
13 September	12	—	—	—	—
17 September	13·4	4·60	40	33·5	2·7
24 September	13·6	—	—	—	—

The puerperium was uneventful and the patient was discharged from hospital on the 10th postpartum day with a haemoglobin of 13·1 g.%. The results of blood examinations in this case were as follows:

Date	*RBC millions per c.mm.*	*Hb. g.%*	*PCV %*	*MCV c. microns*	*MCHC %*	*Reticulocytes %*
13 August	3·6	10·0	33	93	31	—
16 August	—	—	—	—	—	1·5
17 August	—	11	33	—	—	1·6
18 August	—	11·2	—	—	—	1·3
20 August	—	11·4	37	—	—	2·1
21 August	—	11·0	34	—	—	2·4
24 August	—	12·0	—	—	—	2·5
27 August	—	11·6	35	—	—	5·7
28 August	—	12·6	—	—	—	4·0
29 August	—	13·6	41	—	33	6·5
31 August	—	11·0	37	—	30	3·0
1 September	—	11·3	37	—	—	3·0
7 September	—	13·1	—	—	—	1·8

Case 7

Mrs. L.A., age 36 years, para 1, gravida 2. This patient was first seen at the antenatal clinic on 23 February 1956, when she was approximately 14 weeks pregnant. Her haemoglobin was 8·8 g.%. Because of this low haemoglobin the patient received oral iron therapy. On 27 March the haemoglobin had risen to 10·8 g.%. At this stage the patient had a slight vaginal bleeding. She was put to bed and treated conservatively as a threatened abortion. On 22 May the haemoglobin was 10·6 g.%.

Eventually on 23 August the patient was admitted to hospital for investigation. Her previous pregnancy in 1951 was apparently normal. During the early weeks of the present pregnancy she complained of dizziness. There were no gastro-intestinal symptoms.

TREATMENT

Crude liver administered parenterally is occasionally effective, but many cases prove to be refractory.[4,3]

The reported results of therapy with vitamin B12 have not been encouraging. Ungley,[20] Bethell *et al.*[21] and Day *et al.*[22] have all treated cases with vitamin B 12 unsuccessfully. These cases, however, responded to folic acid. Successful therapy with vitamin B 12 is reported from India by Patel and Kocher[7] and Chaudhuri.[8] They maintain that the failure to respond is due to ineffective dosage.

Folic acid seems to be the treatment of choice in the megaloblastic anaemia of pregnancy both during the antenatal and postpartum periods.[4,19]

Of the 7 cases here reported, 6 were treated with folic acid with good response. Case 1 was treated with vitamin B 12, but the rise in the haemoglobin level followed soon after the blood transfusion. This haemoglobin level, however, was maintained on therapy with vitamin B 12.

Blood transfusion was used in 5 cases. This was instituted mainly because of a low haemoglobin near term or because premature labour was threatening. Blood transfusion was also resorted to in cases of postpartum haemorrhage. No adverse reactions were noted during the administration of the blood.

Blood transfusions is the only method whereby the haemoglobin level can be restored hurriedly. It should be used in the cases where the diagnosis has been delayed or overlooked and the pregnancy is near term or the patient actually in labour. An antepartum or post-partum haemorrhage superimposed upon the anaemia may prove fatal. Administration of the blood must be extremely slow and the patient observed carefully for signs of impending cardiac embarrassment.

DISCUSSION

Megaloblastic anaemia of pregnancy is most certainly commoner in the antenatal period than the literature suggests. These cases are not diagnosed because the medical officer often ignores the haemoglobin report and retorts that the patient does not appear 'clinically' anaemic.

Thorough examination of the patient during the antenatal period is essential. Routine haemoglobin estimations must be made at the first visit to the doctor or clinic and then repeated at approximately monthly intervals. If the haemoglobin is found to be low or diminishing rapidly the anaemia should be thoroughly investigated. The difficulty arises when one attempts to define the normal haemoglobin level in pregnancy. The process of haemodilution during pregnancy has always been regarded as producing a 'physiological anaemia' and the lower limit of the normal haemoglobin level is taken to be 10 g.%.[15,23,24] From our observations we feel that a patient with a haemoglobin of 11 g.% or less requires to be observed, and certainly investigated if the haemoglobin level drops any further, particularly while on iron supplements.

It must be remembered that often macrocytes are not seen in the peripheral blood and the case is regarded as an iron-deficiency anaemia, when yet a bone-marrow examination is typical of a megaloblastic anaemia.

Many workers advise that the anaemic patient should be treated with supplementary iron, and if there is no response within 3-4 weeks then a marrow examination should be made. This practice may be adhered to in the non-pregnant patient or in very early pregnancy; but during the middle or last trimester of pregnancy time does not allow for delay in establishing a diagnosis. Correct therapy must be instituted early in order that a normal pregnancy may be maintained. The danger of premature labour and ante-, intra-, or postpartum haemorrhage may prove embarrassing to an anaemic patient, and the puerperium is often fraught with complications in the untreated or inadequately treated case.

SUMMARY

1. The literature of megaloblastic anaemia is briefly reviewed.

2. There are but few cases of megaloblastic anaemia reported as occurring in the antenatal period.

3. Seven cases of megaloblastic anaemia in the antenatal period are described.

4. The diagnosis and treatment is discussed.

5. A plea is made for the early diagnosis and treatment of anaemia of pregnancy.

I am indebted to Prof. O. S. Heyns, Dr. L. van Dongen and Dr. A. Naylor for allowing me to investigate and treat these cases. I should also like to thank the staff of the South African Institute for Medical Research, particularly that of the Department of Haematology, where the laboratory investigations were carried out.

REFERENCES

1. Channing, W. (1842): New. Engl. Quart. J. Med. Surg., **1**, 157.
2. Osler, W. (1919): Brit. Med. J., **1**, 1.
3. Davidson, L. S. P., Davis, L. J. and Innes, J. (1942): *Ibid.*, **2**, 31.
4. Scott, J. M. (1954): J. Obstet. Gynaec. Brit. Emp., **61**, 646.
5. Stevenson, E. M. K. (1938): Trans. Edinb. Obstet. Soc., **58**, 81.
6. Thompson, R. B. and Ungley, C. C. (1951): Quart. J. Med. **20**, 187.
7. Patel, J. C. and Kocher, B. R. (1950): Brit. Med. J., **1**, 924
8. Chaudhuri, S. (1951): *Ibid.*, **2**, 825.
9. Cohen, I. (1953): S. Afr. Med. J., **27**, 627.
10. Adams, E. B. and Wilmot, A. J. (1953): *Ibid.*, **27**, 1028.
11. Evans, W. (1929): Lancet, **1**, 14.
12. Boycott, J. A. (1936): *Ibid.*, **1**, 1165.
13. Reid, W. J. S. and Mackintosh, J. M. (1937): Lancet, **1**, 43.
14. Davidson, L. S. P., Girdwood, R. H. and Clark, J. R. (1948): Brit. Med. J., **1**, 819.
15. Whitby, L. E. H. and Britton, C. J. C. (1953): *Disorders of the Blood.* London: Churchill.
16. Clark, J. R. (1952): Edinb. Med. J., **59**, 274.
17. Miller, H. G. and Studdert, T. C. (1942): Lancet, **2**, 332.
18. Davidson, L. S. P. and Davis, L. J. (1947): Advanc. Intern. Med., **2**, 481.
19. Badendoch, J., Callender, S. T., Evans, J. R., Turnbull, A. L. and Witts, L. J. (1955): Brit. Med. J., **1**, 1245.
20. Ungley, C. C. (1948): *Ibid.*, **2**, 154.
21. Bethell, F. H., Meyers, M. C. and Weligh, R. B. (1948): J. Lab. Clin. Med., **33**, 1477.
22. Day, L. A., Hall, B. E. and Pease, G. L. (1949): Proc. Mayo Clin., **24**, 149.
23. Dieckman, W. J. (1952): *Toxaemias of Pregnancy.* London: Henry Kimpton.
24. Adair, F. L., Dieckman, W. J. and Grant, K. (1936): Amer. J. Obstet. Gynec., **32**, 560.

CRIPPLING DISORDERS IN THE BIBLE

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'And Jonathan . . . had a son that was lame of his feet'
2 *Sam.* 4:4.

The commonest orthopaedic causes of crippling today are tuberculosis of bones and joints, bony injuries, arthritis, poliomyelitis and cerebral palsy. A hundred years ago rickets would also have figured largely in this regard. A thousand years ago and more, all these conditions must have been very common, though it is very doubtful whether gross rickets occurred in the Middle East during biblical times. Blaxland Stubbs[1] writes: 'So far as diseases are concerned, we can say that the Egyptians had them all (including tuberculosis, arthritis and dental caries) with the almost certain exception of rickets and syphilis'. The large amount of sunshine in Middle East countries may have been responsible for this absence of rickets, especially since the available evidence[2] indicates that children were not overclothed and, in Egypt at any rate, went naked (except for sandals) for the first 5 years of life. The etching shown in Fig. 1 clearly indicates the lack of clothing of the young lad.

As regards tuberculosis, it is impossible to establish whether or not this is mentioned in the scriptures, although the reference in Lev. 21:20 to a 'crookbackt' and 'dwarf' could be interpreted in this light. Certainly tuberculosis did occur in antiquity, for we have unmistakable evidence of a Pott's spine in an Egyptian mummy.[3]

Fractured limbs are mentioned in the Bible, Lev. 21:19 noting that the 'brokenfooted' and the 'brokenhanded' were not permitted to serve in the holy sanctuary. The 5-year-old Mephibosheth (2 Sam. 4:4.) apparently had a crippling disease affecting both his legs, and, as I shall attempt to show, his fall resulted in further disability—presumably due to his sustaining a fracture.

Other forms of fracture are also noted in the Bible, Abimelech, Goliath and Sisera sustained fractured skulls. Eli the priest died of a fractured cervical spine, and both Ahazia (2 Kings 1:2) and Eutychus (Acts 20:9) fell out of windows and sustained incapacitating fractures.

Crucifixion, which was a purely Roman practice, was a slow form of death. In order to accelerate dissolution, the Romans were wont to fracture the legs of the victims. This they did to the two men crucified with Jesus (John 19 : 32).

Ezekiel speaks figuratively of fractures: 'I have broken the arm of Pharaoh, king of Egypt; and, lo, it shall not be bound up to be healed . . .' (Ezek. 30 : 21).

We do not know what injury Jacob suffered while he was wrestling with an angel (Gen. 32 : 24), and we can certainly never know, for the story is a myth. He sustained some form of injury to his thigh, and etiological suggestions include an injured sciatic nerve, a ruptured psoas muscle, a dislocated hip, and a slipped lumbar vertebral disc. The diagnosis of a fractured femur seems as good as any, although the fact that healing occurred after exposure of the injured member to the sun (Gen. 32 : 31) would militate against this diagnosis. On the other hand, his injury is very similar to that related in another myth: the thigh injury (? fractured femur) of Jesus when he jumped from the summit of Mount Tabor—which incident is commemorated by the presence of a monastery at the site from which Jesus is supposed to have leaped. St. Jerome says that Jesus was deformed.[4]

Cerebral palsy is mentioned both generally and specifically in the New Testament. Luke 7 : 21 and Matt. 15 : 30 describe how Jesus healed many who were lame (some presumably with cerebral palsy) and Philip (Acts 8 : 7) performed similar feats. Peter describes an actual instance: 'And a certain man lame from his mother's womb was carried, whom they laid daily at the gate of the temple . . . to ask alms . . . Then Peter said . . . rise up and walk. And he took him by the right hand and lifted him up: and immediately his feet and ancle bones received strength. And he leaping up stood, and walked . . . '(Acts 3 : 2). The reference to his feet rather than his hands would suggest that the primary lesion was a paraplegia. An almost exactly similar instance was ascribed to Paul: 'And there sat a certain man at Lystra, impotent in his feet, being a cripple from his mother's womb, who never had walked . . . (and Paul) . . . said with a loud voice, Stand upright on thy feet. And he leaped and walked' (Acts 14 : 8).

According to Brim[5], Erb's palsy can be inferred to have occured in biblical times. Judg. 20 : 15-16 relates the tale of how among a Benjaminite army of 26,000 swordsmen there were 'seven hundred chosen men lefthanded; each one (of whom) could sling stones . . .' Now, as Brim points out, there is no specific Hebrew biblical term for 'lefthanded'. The Hebrew in fact states 'unable to use the right hand', and Brim feels that this means that the right hand was palsied. Attempts have been made to interpret the Hebrew as meaning 'ambidextrous' or 'left-handed', but the Hebrew distinctly states 'Ish itar yad yeminah'—'a man unable to use the right hand'. However, taken to its logical conclusion, we must calculate that 1 in 40 of the soldiers had palsied right arms, and presumably a similar number had palsied left arms. Now no matter how appalling the practice of obstetrics in the tribe of Benjamin, it is inconceivable that they should have 1 in 20 infants born with Erb's palsy. Perhaps the sling-throwers were incapable of using their right hands for this particular purpose simply because they were more practised with the left—i.e., they were in fact left-handed.

Another little-known hero of the Old Testament was Ehud, 'a man left-handed' (Judg. 3 : 15), whom Brim also considers to have been a case of Erb's palsy. Being 'left-handed' he used a subterfuge (hiding a dagger at his right thigh instead of the left—where sentries normally sought concealed weapons) to gain entrance to the palace of 'Eglon king of Moab,' and assassinated this king, who at that time held the Hebrews in tribute.

The matter of poliomyelitis may be introduced by the obscure observation of Prov. 26 : 7, 'the legs of the lame are not equal; . . .' Clearly, this translation of the Hebrew makes no sense when taken in conjunction with the rest of the sentence, 'so is a parable in the mouth of fools.' Admittedly the Hebrew 'dalyu' is a difficult term, but it can probably best be rendered 'weak', 'limp' or 'useless', or alternatively 'misshapen' or 'contorted and contracted', so that Prov. 26 : 7 would be better rendered, 'As useless (or as contorted) as the thighs of a cripple, so is a proverb in the mouth of a fool'.

'And Jonathan . . . had a son that was lame of his feet. He was five years old . . . and his nurse took him up and fled: and it came to pass, as she made haste to flee, that he fell, and became lame' (2 Sam. 4 : 4). Consideration of this English translation leads one to imagine that the introductory sentence might be superfluous, and that Mephibosheth was apparently well until his fall. But the rendering is unfortunate in that it uses only one term 'lame' for two distinct Hebrew terms. The translation would be better written, 'And Jonathan . . . had a son that was lame of his feet . . . and . . . he fell, and became crippled'. In this context it becomes clear that Mephibosheth was lame even before his fall, and that as a result of the fall he suffered further injury—presumably one or more fractures—and thereafter he became crippled. If we postulate that the original lameness was due to poliomyelitis, we can readily understand that the decalcified bones in his legs could snap from the slight trauma of a fall. Of course, his original lameness might have been due to other conditions affecting both lower limbs, such as rheumatoid arthritis, haemophilic joints or muscular dystrophy, but these are distinctly rare in comparison to poliomyelitis. Brim's suggestion[5] that the fall precipitated an attack of poliomyelitis is too far-fetched; so are the suggestions of Preuss[6] and of Rendle Short[7] that Mephibosheth's fall caused an injury to his spinal cord by fracturing his spinal column. A healthy 5-year-old can hardly fracture a spine by falling a foot or two. It seems reasonable to follow the sense of the Hebrew and postulate that he was already lame before he fell, and that thereafter he suffered a further degree of crippling.

There is little doubt that poliomyelitis occurred in antiquity. 'It is probable that poliomyelitis existed in Palestine in an epidemic form during the biblical period.'[8] Its presence in Egypt *circa* 1,200 B.C. can be inferred from the etching on a stele found at Memphis in Upper Egypt (Fig. I). The period shown is from the 19th dynasty and, interestingly enough, the figures depicted are not Egyptian, but more probably emigrants from Syria. The

scene is at the temple of Ashtart—a Syrian goddess whose influence was felt in Egypt from about the middle of the 18th dynasty. She was also known in Babylon as Ishtar, in the Bible as Ashtaroth, and in Greece as Astarte. The 'Keeper of the Door' at the temple is Ruma, who is drawn with pes equinus. Behind him is his wife Imoa and child Ptahemhel.[9]

Fig. I. By courtesy of Ny Carlsberg Glyptotek, Copenhagen.

The pharaohs of the Exodus and of the Oppression are unknown. Many have their advocates—from Thothmes III through Amenhotep II and IV (Ikhnaten) to Ramses II ('The Great') and Merenptah. But the claim of Seti I (died 1,292 B.C.) is as good as any,[10] and this particular pharaoh had a bony malformation of one of his feet. It is difficult to judge whether his mummified foot indicates the presence of equino-varus and club-foot,[3] or equinus and presumptive poliomyelitis.[12]

John 5 : 2-14 describes how Jesus miraculously cured a man who had been crippled for 38 years. The narrative makes it quite clear that his feet were involved to a severe degree, and the remark of Jesus in verse 14 shows that his disability had not been present at birth, but had occurred after the age of (say) 10 years, when a child can reasonably be expected to know right from wrong, and good from evil. Poliomyelitis is thus a reasonable etiological suggestion.

Incidentally, it may be noted that John 5 : 14 is really most revealing, for Jesus admonishes the healed cripple: 'Behold, thou art made whole: sin no more, lest a worse thing come unto thee'. Now the concept that disease followed on sin is well marked in Old Testament writings, but by New Testament times, this concept was being challenged, and other etiological factors were being interposed as the cause of disease—particularly demons. These figure largely in the gospels and in the Acts of the Apostles. So entrenched was the role of demons, that in the 5th century A.D., St. Augustine could write: 'All diseases of Christians are to be ascribed to demons . . . they torment . . . even the guiltless newborn infants'.[13] Thus it is interesting that in John 5 : 14 we note a reversion to the earlier view of the Yahwist etiology of disease.

The same comments may be made concerning the paraplegic (? poliomyelitis) who also developed his disability after the age of discretion. In healing him Jesus said, 'Son, thy sins be forgiven thee' (Mark 2 : 5), and a similar tale is related in Matt. 9 : 2.

Luke 13 : 11 seems to describe kyphosis or kyphoscoliosis: 'And, behold, there was a woman which had a spirit of infirmity eighteen years, and was bowed together, and could in no wise lift up herself . . . And he (Jesus) laid his hands on her: and immediately she was made straight.' Diagnoses such as poliomyelitis and rheumatoid arthritis of the spine come to mind, as well as tuberculosis of the spine, Paget's disease, parkinsonism, and perhaps (but unlikely) late rickets.

Other non-orthopaedic causes of crippling are also mentioned in the scriptures. Jesus cured a man with a withered hand (Matt. 12 : 10). The poor description does not allow of an etiological diagnosis. Poliomyelitis has been hazarded. In the case of Jeroboam (1 Kings 13 : 4) the temporary paralysis of his arm has been postulated as having been caused by an arterial embolus which suddenly became dislodged.[12]

By a long stretch of the imagination, we may consider that Zech. 11 : 17 describes hemiplegia: '. . . his arm shall be clean dried up, and his right eye shall be utterly darkened'.

Lev. 21 : 18 forbids any maimed person from serving in the holy sanctuary. In particular are excluded individuals who are 'sarua'—translated as 'superfluous' ('he that hath any thing superfluous'). The term refers to a person who has a superfluous structure (e.g. polydactyly) and also to one who has an anatomical member (arm, eye, testis) that is larger than its fellow. The term could thus refer, for example, to an individual crippled by a hypertrophied and malformed arm. 2 Sam. 21 : 20 mentions polydactyly.

Neh. 9 : 21 notes the presence of swollen legs (? congestive heart failure, ? beri-beri), and Luke 14 : 2 speaks of 'the dropsy'. Crippling due to infected (? varicose) ulcers on the legs is described in Luke 16 : 20. The beggar Lazarus was evidently so incapacitated by his indolent sores, that he could not walk and had to be carried to sit at the gate of a wealthy man, where the dogs were wont to come and lick at the sores.

Adoni-bezek, a Canaanite king, was crippled by means of having his thumbs and great toes cut off (Judg. 1 :6), a cruelty that he had inflicted previously on 70 subjugated chieftains.

The case of King Asa illustrates that his gangrenous legs[12] failed to heal under the ministrations of his physicians. 'Asa . . . was diseased in his feet . . . yet . . . he sought not to the Lord, but to the physicians. And Asa . . . died . . .' (2 Chron. 16 : 12-13).

REFERENCES

1. Stubbs, S. G. B. (1952): *From Magic to Modern Medicine.* London: C. A. Watts & Co.
2. Castiglioni, A. (1947): *A History of Medicine.* New York: Alfred Knopf.
3. Sigerist, H. E. (1951): *A History of Medicine*, vol. 1. London: Oxford University Press.
4. Graves, R. (1952): *The White Goddess*, p. 332. London: Farber and Farber.
5. Brim, C. J. (1943): J. Nerv. Ment. Dis., **97**, 656.
6. Preuss, J. (1911): *Biblisch Talmudische Medizin.* Berlin: S. Krager.
7. Short, A. R. (1953): *The Bible and Modern Medicine.* London: Paternoster Press.
8. Levy, A. J. (1942): Med. Leaves, **4**, 22.
9. Petersen, O. K. Ny Carlsberg Glyptotek, Copenhagen. Personal communication.
10. Ausubel, N. (1955): *Pictorial History of the Jewish People.* New York: Crown Publishers.
11. Ruhrah, J. (1932): Amer. J. Dis. Child, **43**, 195.
12. Brim, C. J. (1936): *Medicine in the Bible.* New York: Froben Press.
13. Russell, B.A. (1935): *Religion and Science.* London: Thornton, Butterworth.

NEW YEAR MESSAGE FROM THE SECRETARY GENERAL OF THE WORLD MEDICAL ASSOCIATION

In a New Year Message headed 'I believe in this' the Secretary General of the World Medical Association, Dr. Louis H. Bauer, writes:

Promoting World Peace

The words of Dr. Elmer L. Henderson in commenting on the desirability of organizing the WMA and in advancing its objectives would seem true prologue to my remarks, especially when the progress of the association is contrasted with the increasingly perilous political situation in the world today. All doctors are pledged to assist the people of the world, to attain the highest possible level of health and through this objective 'to promote world peace'. The doctor devotes his life to conserving and restoring the mental and physical health of the patient, and in research toward improved methods to accomplish this aim. It is the only profession that concentrates its efforts toward reducing and eventually even eliminating the need of society for its services. In contrast to this we see the politician, and at times even the so-called statesman, committing the people to support policies that result in mutilation, death, disease, starvation and mental anguish of millions.

The 10th General Assembly has recommended that member associations utilize every opportunity to make each individual doctor an ambassador of peace and has suggested that methods involving minimal expense and maximum results in implementing a programme to promote better international relations could include:

Mutual exchange visits of foreign doctors.

Exchange of distinguished medical teachers.

Representation, wherever possible, of all member associations at the annual meeting of each member association.

Holiday exchange programmes between doctors and their families.

It has also been pointed out that the status the doctor has among his patients and in his own community is a strong potential that should be used to its utmost in promoting peace among all people.

The implementation of this programme is an additional means of promoting 'closer ties among the national medical organizations and among the doctors of the world' as well as 'promoting world peace'.

Attaining the Highest Level of Health

It has sometimes been alleged that WMA and doctors in general, oppose the socialization of medicine and social security plans for reasons of personal economic betterment or without a constructive programme which would fill the social responsibility the agencies and organizations promoting social medical programmes strive to accomplish. Such allegations are not based upon fact. The WMA recognizes the need for government and agencies to provide medical care for those unable to meet the economic crisis of illness. It is of the opinion that in every nation there are those who require full protection; those who require partial protection; those who need assistance in saving for the eventuality of illness; and finally, those economically able to provide their own medical care. It recognizes all human beings as being whole and free—and believes that only through encouraging individual responsibility for life's crises and providing the right of free choice to each individual can the dignity of man and his psychic as well as physical welfare be advanced to the highest level of health.

The social security discussions at the 10th General Assembly highlighted such important factors as the increasing cost of medical education and medical care resulting from increased scientific advancement; the economic saving accrued from the use of the more expensive and equally more effective treatments and medicaments; the therapeutic benefits that result when the doctor-patient relationship is unhampered and both patient and doctor are free; and finally, the growing tendency of social agencies to place the system above the individual, especially in medical care and illness, which is a completely individual and personal experience. The Assembly agreed that:

Cost of medical service should be kept as low as is compatible with the best medical care.

Doctors' cooperation in health plans for the medical treatment of those unable to provide care for themselves is essential, but these plans must provide the doctor with the essentials for serving the patient to the best of his ability.

Each national medical association must solve the problems in this field in accordance with the economic, social and professional situation within its country, recognizing the importance of a constructive programme of which the people are advised and their support solicited.

In addition, the General Assembly approved continuation of a programme to obtain national and international recognition of a medical emblem, code of medical ethics in war time and regulations to govern the use of this emblem by civilian doctors and civilian defence units in time of national or international war. This project has been under way since 1953, when efforts were made to have the protection of the Red Cross extended to civilian doctors and civilian defence units. The Red Cross organization pointed out the impossibility of cooperating in this request and suggested that WMA establish an emblem and regulate it for this purpose. In this project it pledged its support, cooperation and guidance.

The 10th General Assembly adopted the suggested emblem—a red serpent and staff on a white field; the serpent represented by a sinuos line with three undulations coiled around a vertical stick; two undulations on the left and one on the right—and approved the 'Code of Medical Ethics in time of war' which is based upon the International Code of Medical Ethics adopted by the General Assembly in 1949. The regulations for the emblem must be drafted, but national member associations are requested to have the emblem and code approved by their membership and begin the necessary procedures for legal recognition within their countries.

ASSOCIATION NEWS : VERENIGINGSNUUS

DISPENSING BY DOCTORS

A round-table conference was held in Johannesburg on 26 November 1956, between representatives of the Pharmaceutical Society of South Africa and the Medical Association of South Africa by mutual arrangement between the two bodies. The meeting followed the suggestion made by the then Minister of Health (Hon. J. F. T. Naudé) at the end of the last session of Parliament that the opportunity afforded by the parliamentary recess should be used for discussions between the medical profession and chemists and druggists concerning the legislation that the Pharmacy Board had advocated restricting the right of registered medical practitioners to dispense their own medicines.

It is not to be confused with meetings that have also taken place between representatives of the South African Medical and Dental Council and the South African Pharmacy Board.

The Medical Association was represented by Drs. Sichel, Struthers, Harvey Pirie, M. Shapiro, Schneider, Turton and Waks (Dr. Tonkin, Secretary of the Association, attending) and the Pharmaceutical Society by Messrs. Kramer, Gavshon, Kuter and Rubenstein (Mr. Righthouse, Secretary of the Society, attending). On the motion of Mr. Kramer, Dr. Sichel was appointed chairman of the meeting.

A full and frank discussion took place, and it was eventually resolved to set up a joint committee consisting of 3 representatives

from each of the two bodies, with power to co-opt, to consider the whole problem as it affects the two organizations in order to try and find a formula which might be mutually acceptable. Mr. Righthouse was appointed as convener, and it was decided that a meeting of the joint committee should be called as soon as the convener received the names of the members appointed by the Medical Association.

It was explained that the Council of the Pharmaceutical Society had passed resolutions deciding (1) to approach the Minister of Health and press for amendments *inter alia* of section 73 of the Medical, Dental and Pharmacy Act (dealing with dispensing by doctors), and (2) to ask for a discussion on the subject with the Federal Council of the Medical Association. These decisions could not be varied until the Council met again, but Mr. Kramer, President of the Pharmaceutical Society, gave an assurance as Chairman of the Executive Committee that his Executive would recommend to the Council of the Society at its next meeting, to be held in Cape Town in April 1957, that action as regards the legislative approach should not be proceeded with until the joint committee now set up had made its report.

PASSING EVENTS : IN DIE VERBYGAAN

Dr. R. Elsdon-Dew, Honorary Director of the Amoebiasis Research Unit of the Council for Scientific and Industrial Research, has been elected a Fellow by the American Society of Tropical Medicine and Hygiene. This award is made 'for meritorius contributions to Tropical Medicine'.

Will the author of the article 'Orbital Implant of Moura Brazil', which has been submitted for publication in this *Journal* kindly communicate with the Editor as soon as possible?

REVIEWS OF BOOKS : BOEKRESENSIES

BING'S NEUROLOGICAL DIAGNOSIS

Bing's Local Diagnosis in Neurological Diseases. Translated, Revised and Enlarged from the Fourteenth German Edition. By Webb Haymaker, M.D., with Chapters by Richard G. Berry, M.D., Bernard S. Epstein, M.D. and Paul I. Yakovlev, M.D. Pp. 478. 225 Illustrations, including 9 in Colour. St. Louis: C.V. Mosby Company. 1956.

Contents: 1. Tracts, Cell Groups and Blood Supply of the Spinal Cord. 2. Spinal Cord Functions. 3. The Localization of Spinal Lesions in the Transverse Plane. 4. Anatomical and Functional Aspects of Spinal Segments. 5. Segmental Localization of Spinal Lesions. 6. Localization of Lesions of the Cervical and Uppermost Thoracic Segments. 7. The Localization of Lesions of Lower Segments of the Spinal Cord. 8. X-Ray Localization of Spinal Tumours. 9. The Structure of the Brain Stem. 10. General Rules for the Localization of Lesions in the Brain Stem. 11. The Localization of Lesions Involving Cranial Nerves IX Through XII. 12. The Localization of Lesions Involving the Facial Nerve. 13. The Localization of Lesions Involving the Acoustic Nerve. 14. Localization of Lesions Involving the Trigeminal Nerve. 15. Localization of Lesions Involving the Extraocular Nerves. 16. Disorders of Cerebellar Origin. 17. The Arterial Supply of the Brain Stem and Cerebellum and Syndromes of Arterial Occlusion. 18. The Cerebral Cortex and Its Motor Pathways. 19. The Localization of Motor and Sensory Disturbances of Cerebral Origin. 20. The Localization of Frontal Lobe Disorders. 21. The Localization of Disturbances of Vision and Pupillary Reflexes. 22. The Localization of Anarthria, Aphasia and Apraxia. 23. The Localization of Extrapyramidal Motor Disorders. 24. The Localization of Lesions of the Thalamus. 25. The Clinical Features of Lesions of the Hypothalamus, Pituitary Gland and Upper Midbrain. 26. Arteries of the Cerebrum and Syndromes of Their Occlusion. 27. Localization of Aneurysms of Cerebral Arteries. 28. Intracranial Tumors: Location, Type, Cerebrospinal Fluid. 29. X-ray Localization of Intracranial Lesions, Especially Tumors. 30. The Use of Electroencephalography in Neurological Diagnosis.

There must be many neurologists still practising who remember the days when the old 'Bing' was the book they most frequently turned to when puzzled over some difficult point in localization. The present edition of Bing's Handbook, brought up to date by Dr. Haymaker, is a tribute to a great neurological clinician.

There have been many Introductions to Neurology and many books on Neuro-anatomy in recent years but none have been better than Bing's Kompendium. However, it is nearly 50 years since the first edition was printed and even in neurology changes occur in half a century. One has only to think of air encephalography and of angiography to realize how very much more of the coarse structure of the intracranial contents is readily visualized and how, consequently, our knowledge of localized syndromes has enlarged. However, it is just this easy short-cutting approach to a clinical problem which has proved disastrous to a reasoned survey and careful bedside diagnosis in difficult neurological cases, and for the very reason that Bing has always advocated the tackling of problems from the basis of a sound knowledge of anatomy and physiology this new edition of his work is most welcome.

It is difficult to praise this book too highly. Gone are most of the dreary Germanic illustrations of the earlier editions, and in their place are clear photographs and diagrams. The rather formidable diagram of cortical speech-centres is an exception; in this there is a distinct pre-Goldstein mannerism on the background of a brain which looks distinctly Neanderthalic. The vascular syndromes of the brain-stem are treated with Gallic imaginativeness, and it is a pity that the section of visual field defects was not enlarged and that more emphasis was not laid on the great importance of accurate field assessment. But the book as a whole is one of the very greatest value to every practising neurologist and everyone dealing with neurological medicine, and it is unreservedly recommended to them.

J.MacW.MacG.

SYNOPSIS OF PSYCHIATRY

A Synopsis of Contemporary Psychiatry. By George A. Ulett, B.A., M.S., Ph.D., M.D. and D. Wells Goodrich, M.D. Pp. 243. £2 4s. 9d. St Louis: The C.V. Mosby Company. 1956.

Contents: I. Introduction. II. History of Psychiatry Thought. *History Taking and Diagnostic Procedures.* III. Examination of the Patient. IV. The Initial Psychiatric Interview. V. The Complete Case Study. VI. General Physical and Neurological Examination. VII. The Problem of Examining the Patient for Aphasia, Agnosia and Apraxia. VIII. Electroencephalographic Examination. IX. Psychological Examination. X. Psychodynamic Concepts of Personality Development. *Clinical Syndromes.* XI. The Problem of Classification. XII. Standard Nomenclature, Diseases of the Psycho-Biologic Unit as prepared by the Committee on Nomenclature and Statistics of the American Psychiatric Association. XIII. Disorders caused by or Associated with Impairment of Brain Tissue Function. XIV. Disorders of Psychogenic Origin (or without clearly defined physical Cause or structural change in the brain). XV. Mental Deficiency. XVI. Child Psychiatry. *Therapeutic Measures.* XVII. The Psychiatric Treatment Team. XVIII. Individual Psychotherapy. XIX. Group Therapy. XX. The Convulsive Therapies. XXI. Insulin Therapy. XXII. Psychosurgery. XXIII. Drug Therapies. XXIV. Hydrotherapy. XXV. Management of Suicidal Patients. XXVI. Management of Civilian Disaster. XXVII. Management of Psychiatric Problems in the Military Setting. XXVIII. Forensic Psychiatry. XXIX. The Psychiatrist and Mental Health.

This book is designed for the use of psychiatric interns and nurses and as such it contains a remarkable amount of up-to-date material in a highly compressed form. The authors make it clear that the volume is only put forward as a ready-reference book for those who are starting to deal with psychiatric problems, but as a *vade mecum* for these tyros it should be useful. The approach is that of the orthodox practical type and although psychotherapeutic measures are advocated there is no space for any detailed advice along these lines. The physical treatments are more thoroughly dealt with here and there is an admirable note of restraint, so that one is left with the impression that the book has been written by those who are familiar with hospital psychiatric practice and who have not been unduly influenced either by the psycho-analytical or by the 'shock-'em-out-of-it schools.

As regards the drug control of psychiatric states it is a pleasure

to see a restrained yet knowledgeable outlook. Chlorpromazine and reserpine are judiciously dealt with but cortisone, perhaps wisely, receives no mention.

It is a pity that such leave-overs of the bad old days of mental-hospital practice (one can hardly call it treatment) such as 'wet-sheet packing' and 'stimulating douches' have found any place in such a book, but the authors may be making a concession to conditions which still, unfortunately, exist in some mental hospitals.

If this book is used as it is intended, and if the admirable 'suggested reading' titles are used in conjunction with it, then it will be found to be a stimulating and helpful pocket-book for the psychiatric beginner.

J.MacW.Mac.G.

HYDATIDIFORM MOLE AND CHORIOCARCINOMA

Tumors of the Female Sex Organs. Part 1. *Hydatidiform Mole and Choriocarcinoma.* By Arthur T. Hertig, M.D. and Hazel Mansell, M.B., B.S. Pp. 62. Figures 65. Colour Plates 2. $1.00. Washington: Armed Forces Institute of Pathology. 1956.

Contents: Hydatidiform Mole and Choriocarcinoma of the Uterus. Hydatidiform Mole and Choriocarcinoma, Extrauterine. References.

This is an atlas of the pathology of hydatidiform mole and choriocarcinoma—the first of a series dealing with tumours of the female sex-organs.

Hydatidiform mole is a rare condition, choriocarcinoma even more so. But both these conditions provide us with a stimulus to thought out of all proportion to the frequency of their occurrence. Trophoblast, from which these tumours develop, exhibit a marked invasive property. Why, ask the author, should early trophoblast of the 7-day ovum invade rapidly and progressively while its more mature derivative usually comes to rest within a millimetre or two of the myometrium? Why should trophoblast be transported to the lungs but only that of the choriocarcinoma be capable of sustained growth? If we knew the answers to these two simple questions, the phenomena of invasion and metastasis—the two fundamental factors which make cancer differ from normal tissue—would be understood vastly better than they are now. In the properties of the normal trophoblast lie locked up many secrets of cancer.

From time to time one hears of the cure of a patient with choriocarcinoma and one wonders about the accuracy of the diagnosis. One may quote the following passage from this book: 'The trophoblast of even the most potentially malignant moles never, in the authors' experience, looks quite like the prophoblast of the choriocarcinoma which may follow it. Unless this fact is clearly realized by the pathologists and clinicians alike uteri will be removed unnecessarily'. The care to be exercised by the pathologist in the interpretation of the histological picture is further stressed in the following statement: 'In order to evaluate fully the morphologic malignant potential of any hydatidiform mole, tissue from at least 8 to 10 different areas of the specimen must be taken for microscopic section. Clusters of villi, not merely individual vesicles, must therefore be selected. This is necessary because within the molar mass the most atypical trophoblast often lies between the vesicles or on the surface of blood clot. Hence sections of the blood clot are important in the evaluation of a mole'.

This atlas contains much that is of interest to both gynaecologist and pathologist. The pictures are first-rate. One looks forward to the appearance of the remaining parts of this series on gynaecological tumours.

E.M.S.

HISTORY OF PUBLIC HEALTH

A Short History of Public Health. By C. Fraser Brockington, M.A., M.D., D.P.H., B.Chir., M.Sc. Pp. vii + 235. 15s. net. London: J. & A. Churchill Ltd. 1956.

Contents: Part I. The Growth of Public Health. I. The Early Pioneers of Health in the Eighteenth Century. II. First Steps in National Organization of Public Health, 1800-1837. III. Early Sanitary Reform, 1838-1848. IV. Essays in Central Control, 1848-1870. V. Local Government Begins, 1870-1900. VI. An Approach to Personal Hygiene, 1900-1918. VII. The Inter-war Period. VIII. Post World War II. *Part II. Special Aspects of the Growth* of Public Health. IX. Economic and Social Changes and their effect upon Mortality and Population during the Past Hundred Years. X. Housing during the Past Hundred Years. XI. The Growth of Services for Maternital and Child Health. XII. The Growth of Care for Neglected Children. XIII. The Growth of Services for Disorders of the Mind. XIV. The Growth of Services to Control Tuberculosis. XV. The Growth of Services to Control Venereal Diseases. XVI. The Growth of Care for the Aged. Conclusion. Bibliography. Index.

This lucidly written and interesting short history of British public health by C. Fraser Brockington should be read by all interested in the progress of public health.

The development and growth of all aspects of British public health are most refreshingly traced and non-medical lay persons, such as Dickens, Chadwick and others, are given their rightful place as pioneers in bringing to light and to the notice of the public the abominable slums and deplorable living conditions of the working classes in the Britain of the last century.

History has an unhappy habit of repeating itself, and apart from the general interest and the manner in which this work has been compiled, the lessons to be learnt may be quite readily be applicable to conditions which might well occur in this country of ours as the result of our own industrial revolution.

Similarly, the administration of remedies resulting eventually in the passing of the National Health Act of 1946 by the British Parliament, could be pondered upon, studied and possibly applied in such a manner as to fit local conditions.

The index appears reasonably full, but the quality of the paper leaves much to be desired.

A most readable and interesting book which can be highly recommended.

E.D.C.

PRACTICAL THERAPEUTICS

A Course in Practical Therapeutics. Third Edition. By Martin Emil Rehfuss, M.D., F.A.C.P., LL.D. (Hon.) and Alison Howe Price, A.B., M.D. Pp. xviii + 972, with 101 Plates. 120s. London: Baillière, Tindall & Cox Ltd. 1956.

Contents: Section I. General Therapeutic Principles. Introduction. Planning a Program. Diagnostic Survey. A Definite Plan. Outlining a Plan. Adjustment of the Patient. Prescription Writing. Capsules. Drops. Powders. Suppositories. Liquids. Dietary Principles. Dietary Indications in Disease. Methods of Arranging the Dietary. Nursing Problems of Interest to the Physician. Contents of the Physcian's Bag. *Section II. Symptomatic Therapy.* Acute Abdominal Emergencies. Acidosis. Alkalosis. Anorexia. Anuria. Ascites. Backache. Coma. Constipation. Convulsions. Cough. Cyanosis. Diarrhea and Dysentery. Drowsiness and Somnolence. Edema. Epistaxis. Fever. Flatulence and Aerophagia. Headache. Hematuria. Hemoptysis. Insomnia. Itching (Pruritis). Jaundice. Muscular Spasm. Myasthenia Gravis. Nausea and Vomiting. Pain. Priapism. Shock. Singultus (Hiccough). Sunburn. Tetany. Tic. Vertigo. *Section III. Treatment of Specific Disorders.* Vitamin Deficiency States and Nutritional Disorders. Vitamin A. Vitamin B. Complex. Thiamine. Riboflavin. Niacinamide. Kwashiorkor. Pyridoxine. Pantothenic Acid. Biotin. Choline. Inositol. Folic Acid. Para-Amino-Benzoic Acid. Ascorbic Acid. Vitamin D. Vitamin E. Vitamin K. Vitamin$_{12}$ B. Obesity. Digestive Tract Disorders: Diseases of the Mouth. Esophageal Disease. Diseases of the Stomach. Diseases of the Intestines. Diseases of the Liver and Biliary Tract. Diseases of Blood and Blood-Forming Organs. Diseases of the Heart. Peripheral Vascular Diseases. Diseases of the Kidneys. Venereal Diseases. Respiratory Diseases. Arthritis. Allergic Disorders. Physical Agents and Poisons. Infectious Diseases. Systemic Myocoses. Endocrine Disorders. *Section IV. Special Treatment.* Antibiotics. Steriod Therapy. Ocular Therapeutics. Nasal Therapeutics. Otological Therapeutics. Dermatological Therapeutics. Psychotherapy. Psychosomatic Medicine. Specific Psychiatric Syndromes. Industrial Therapeutics. Preoperative Treatment. Body Water and Electrolytes. Therapeutic Use of Parenteral Solutions. Therapy of Postoperative Complications. Oxygen Therapy. Radioactive Isotopes. Radiation Therapy. Physical Medicine. Medical Rehabilitation. Occupational Therapy. Pediatric Therapeutics. Gynecological Therapeutics. Index.

This book is the work of 24 contributors and a glance at the summary of contents will indicate that it covers a great deal of ground. It embraces much more than the title suggests, for succint accounts of clinical features and differential diagnosis accompany the notes on treatment. With the incorporation of a variety of therapeutic advances (new insulins, antibiotics, steroid therapy, radioactive isotopes, etc.), the book now appears in its 3rd edition.

The type is good and the material systematically arranged; the text is lucid, the index excellent, and numerous full-page schematic diagrams summarize salient aspects of common disorders; a uniformity of approach permits easy and rapid reference. The actions and toxicity of drugs are emphasized throughout, and the authors are careful to avoid the use of remedies which are not yet of established value.

Since the doctor has often to deal with a series of complaints before a diagnosis is made, the section on symptomatic therapy

finds a logical place in the early chapters. The problem of headache is particularly well presented.

The treatment of specific disorders, which constitute 2/3rds of the book, is comprehensive and informative. It is unavoidable, in a work of this kind, that the individual physician may find many points open to criticism. For example, routine digitalization is not recommended prior to the administration of quinidine in cases of auricular flutter; some would regard the omission of intrathecal therapy as unwise in pneumococcal and influenzal meningitis; and many would disagree with the statement that patients with 'bilateral tuberculous disease of an exudative or caseous nature' are suitable for treatment by pneumoperitoneum.

On the whole, however, the authors succeed admirably in their essential purpose, to present the modern treatment of disease in the simplest form. It is unfortunate that the price of the book places it beyond the reach of the average student.

P.M.

PREMARITAL MEDICAL CONSULTATION

The Premarital Consultation—A Manual for Physicians. By Abraham Stone, M.D. and Lena Levine, M.D. Pp. v + 90. 11 Figures. $3.00. New York and London: Grune & Stratton, Inc. 1956.

Contents: Introduction. Premarital History. Examination. Interview: Sexual Adjustment—Family Planning and Contraceptive Methods—Social and Emotional Factors in Marriage. Genetics. Appendix: 1. Contraceptive Technique: The Vaginal Diaphragm. 2. Marriage Laws of the States. 3. Birth Control Laws. Bibliography. National Organizations. Index.

Premarital consultation with the family doctor is not common practice in this country. There is no doubt that much misunderstanding, ignorance and unhappiness could be avoided if engaged couples would talk things over with their doctors before the wedding day. All organizations engaged in guidance in marriage problems should encourage such premarital medical consultation.

This small book has been written for the general practitioner, who may find it rather elementary in parts. However, it contains much useful information, which is clearly presented. The chapter on contraceptive technique could well have been a little more detailed. The laws concerning marriage and birth control which are discussed at the end of the book apply to the United States only.

Although written for the doctor this book may be read with profit by the intelligent layman and laywoman.

E.M.S.

PHYSIOLOGY OF THE OCULAR AND CEREBROSPINAL FLUIDS

Physiology of the Ocular and Cerebrospinal Fluids. By Hugh Davson, D.Sc. (Lond.). Pp. viii + 388. 109 Illustrations. 65s. net. London: J. & A. Churchill Ltd. 1956.

Contents: I. Morphological Aspects of the Intraocular Fluid. II. Morphological Aspects of the Cerebrospinal Fluid. III. Chemical Composition and Secretory Nature of the Fluids. IV. The Exchange of Substances between the Blood and Aqueous Humour. V. The Blood-Aqueous and Blood-Cerebrospinal Fluid Barriers. VI. The Relationship between the Cerebrospinal Fluid and the Nervous Tissue. VII. Breakdown of the Barriers and the Protein Content of the Fluids. VIII. Special Aspects of the Chemical Composition of the Fluids. IX. The Fluid-Pressures. Index.

Dr. Davson believes that the mode of origin of the intra-ocular and cerebrospinal fluids is fundamentally the same and that the two fluids have so much in common that they may conveniently be studied together; thus ophthalmologist and neurologist may learn from each other's investigations. The thesis is well sustained in this excellent monograph.

Starting with a detailed description of the vascular systems of the eyeball and brain, the author proceeds to a presentation of the evidence that both intra-ocular and cerebrospinal fluids are true secretions. The concepts of blood-aqueous and blood-cerebrospinal-fluid barriers are elaborated, and the circulation and reabsorption of both fluids are described. The composition of the fluids is studied in detail, with particular reference to the significance of variations, and the biophysical principles involved in the maintenance of the fluid pressures are outlined. As in most of his previous writing, Davson's approach is that of the general physiologist; fundamental principles are illustrated by reference to whichever species provide the best examples.

Each chapter is followed by a comprehensive and up-to-date bibliography, and the general presentation is of the high standard which we have come to expect from J. & A. Churchill. The book is not designed primarily for the clinician but will be invaluable to everyone pursuing research on either the intra-ocular or the cerebrospinal fluid.

A.W.S.

INTRACARDIAC PRESSURES

Cardiac Pressures and Pulses. By Aldo A. Luisada, M.D. and Chi Kong Liu, M.D. Pp. vii + 116. 51 Figures. $6.00. New York and London: Grune & Stratton, Inc. 1956.

Contents: Introduction. 1. The Cardiac Cycle. 2. Technique of Catheterization. 3. Normal Pressures of the Cardiac Chambers and Large Vessels. 4. Normal Patterns of Pressure in the Cardiac Chambers and Large Vessels. 5. Abnormal Pressure Patterns. 6. Artifacts. 7. Formulas Used in Cardiac Catheterization. Bibliography. Index.

This book has succeeded very well in correlating the findings of pressure and pulse recordings obtained from many sources by intracardiac studies. Left heart catheterization is also mentioned and a very useful chapter on furmulae is included in this useful volume.

Anyone who has worked in this field knows how easily artefacts are introduced—often making detailed study of the pressure curves very difficult. Too often wave changes have been analyzed at length, and some plausible explanation offered for this or that wave form, when a loose connection, an air bubble, damping, or catheter whip, has been responsible for the unusual tracing. It is stressed, too, that patterns recorded with the catheter wedged in the pulmonary capillaries present a wide variation even in normal subjects.

Your reviewer was glad to read that recordings of the wave due to the regurgitant jet in mitral incompetence, are inconstant—so that while its presence is interesting, its absence is not unusual in mitral incompetence.

Good examples are shown of the pulmonic 'shudder' in pulmonary stenosis.

Perhaps the only criticism of this very fine manual is the unnecessary repetition—but this is not altogether a fault. The book contains a wealth of information.

M.N.

SEX PROBLEMS

Sex Problems and Personal Relationships. By E. Parkinson Smith and A. Graham Ikin, M.A., M.Sc. Pp. 149. 10s. net. London: Messrs. William Heinemann Medical Books Ltd. 1956.

Contents: Preface. Part One. 1. The Task of Sex Education To-day. 2. Christianity and Sex. 3. Sex and Friendship. 4. Marriage and Parenthood. 5. The 'Mixed' Marriage. 6. Sex and Religion in the Conflict of Adolescence. Part Two. 7. Personal Relationships and Sex Problems. 8. Sex, Motherhood and Society 9. Problems During Courtship or How to be Happy While Courting. 10. Critical Periods in Marriage or How to be Happy While Married. 11. Homosexuality and Family Life. 12. Cultural Aspects of Marriage. 13. Cultural Values in the Atomic Age. Index.

This book is in two parts. The first deals primarily with the problems facing the younger generation. These are dealt with in a clear and sympathetic manner by the first author, who takes the view that the problem facing most adolescents is not only sexual but also religious.

The second part includes much for the more mature and is dealt with by the second author. Many of the difficulties of the more mature are the result of ignorance or mistakes during the childish or adolescent stages.

This book is not just another guide to 'married love' but is intended to help the intelligent reader regarding sexual problems. It is a religious book, but is broadly religious and can offend no one. It is intended for the understanding and older adolescent, for young persons married or about to be married, and for the older generation. For the latter it will be particularly helpful in instructing the former.

This little book written by a man and a woman will be of great value to those of both sexes who are concerned about the philosophy of sex.

P.J.M.R.

A NEW JOURNAL IN CLINICAL CHEMISTRY

Clinica Chemica Acta. International Journal of Clinical Chemistry. Cleaver-Hume Press Ltd., London, W.8. for Elsevier Publishing Company—Amsterdam—London—New York—Princeton. Vol. I, 1956 (6 nos.) 90s. Vol II, 1957, the same.

Vol. I, No. 1 *p.p.* 1-100, *January* 1956.

Contents: Introduction. Resolution. Serum polysaccharides in diabetes mellitus, by D. V. Andreani and C. H. Gray (London). Abnormal globulins in some neoplastic diseases, by B. Jirgensons and J. A. Cooper (Houston, Tex.). Homologous serum proteins and their role in phenomena of increased capillary permeability in inflammation, by T. S. Paskhina (Moscow). Direct actions of k-strophantin on cellular metabolism of the kidney and their consequences for the formation of urine, by J. Frey (Freiburg) (i.Br). Electro-chromograms of human bile, by J. C. M. Verschure (Utrecht). Les acides cétoniques du sang et de l'urine. Étude analytique: identification d'hydrazones nouvelles: applications cliniques, par G. Biserte et B. Dassonville (Lille). Phosphohexoisomerase, Phosphoriboisomerase und Milchsäuredehydrogenase im Liquor cerebrospinalis, von F. H. Bruns, W. Jacob und F. Weverinck (Düsseldorf). Photo-disintegration of the deuteron for deuterium analysis, by E. Odeblad (Stockholm). Paper chromatography of urinary amino acids, by J. Awapara and Y. Sato (Houston, Tex.). The estimation of mercury in urine di-β-naphthylthiocarbazone, by H. Leach, E. G. Evans and W. R. C. Crimmin (Bangor). The cation-induced flocculation of serum proteins, by N. Ressler and S. D. Jacobson (Eloise, Mich.). Les mélanogènes dans un cas de mélanurie, par H. Wachsmuth (Anvers). Book Review. Announcements.

Hitherto the clinical chemist has not had a journal of his own and records of his efforts are scattered in general medical journals, biochemical journals and in other journals, with the other divisions of pathology and with endocrinology. This was felt strongly at the 1954 International Congress of Clinical Chemistry and this new journal has been started in an attempt to meet these needs.

Its intention is to aid in the mutual understanding of chemists and clinicians and to provide for exchange of information between laboratories in different countries with consequent standardization of methods where this is desirable.

The names of the editorial and advisory boards are a guarantee that the contributions will be of high standard; among them appear such well known figures in the English-speaking world as Van Slyke, McCance, Maclagan and C. P. Stewart. Most of the articles are in English but some are in French and German; summaries are given in these languages and in Russian.

The contents of the first 3 numbers show that this is not a mere technical journal but is largely devoted to the presentation of research, most of it centred on the laboratory rather than on the bedside. Only a few of the articles have as their main concern analytical methods but some of these are of importance.

This journal should certainly be available in the libraries of medical schools and in laboratories where active work in clinical chemistry is in progress.

G.C.L.

DR. JOHNSON'S CASE

A Doctor Returns. Being the Third Part of 'A Publisher Presents Himself'. By Donald McI. Johnson. Pp. 256. 16s. London: Christopher Johnson Publishers Ltd. 1956.

Contents: I. A Psychotic Episode. II. A Conspiracy of Silence. III. A Double Event. IV. This is the Law. V. Humpty Dumpty. VI. A Doctor Returns. VII. Indian Hemp: A Social Menace. VIII. The Mystery of Pont Saint Esprit. IX. Anticlimax. X. Further Anticlimax. XI. The Hallucinogenic Drugs: A Neglected Aspect. XII. Scotland Yard. XIII. And the Prime Minister. XIV. Despotism is Unteachable. XV. I Publish my Findings. XVI. Wot! No Villain? XVII. The Eigth Square At Last. XVIII. The Problems of Mental Illness. XIX. A Solution. XX. The Case of Colonel Drummond.

In the middle of October 1950 the author was confined in a mental hospital. Apparently his behaviour had been sufficiently strange to warrant certification and as he describes his peculiar thoughts and grandiose ideas it is difficult not to accept the fact that his medical advisors acted wisely in so doing. Within a short time he improved remarkably and within 6 weeks he was fit enough to return home.

Most of us would have been thankful to be regarded as fit for normal society. Not so Dr. Johnson. He believed that he should never have been certified. Perhaps he was right. Perhaps he should have been detained in an 'observation ward' of a general hospital. Those of us who have had to handle this sort of problem can see the rights and wrongs of both sides. His certification could not be challenged in law despite certain slight irregularities. But Dr. Johnson sets out on a crusade to see that this sort of thing does not happen to other unfortunates. And what a nuisance he makes of himself! One can readily understand his M.P.'s reluctance to see him and to ask further questions in the House! And on his own election to Parliament he is able to carry on the fight on his own behalf.

He believed that he had been poisoned. As evidence of this he cited the fact that his wife suffered from similar symptoms. Also that the symptoms could have been produced by each, or a combination, of two hallucinogenic drugs. There is no other proof of the poison so it is not surprising that no one was prepared to take his story seriously. He will not allow the possibility that he was in fact suffering from hallucinations due to other cause. His arguments are all one-sided and he argues all the time from what may well be a false premise. He may be right but he may equally well be wrong. As an independent person reading the evidence as presented by the author. I cannot help feeling that the author is probably in the wrong!

That our outlook on mental disease is old-fashioned and in need of reform is probably correct. That the law may be old-fashioned and in need of reform is probably also correct. (In fact a Royal Commission was at the time taking evidence in this regard.) But many would not accept Dr. Johnson's case as a good one to cite in a discussion of this kind. Realizing the difficulties inherent in this sort of problem (medical, legal, mental and physical), many of us would regard the author as being dsitinctly fortunate in being able to be released so soon and to be able to take up life again with so much success.

C.M.

CYSTECTOMY FOR CANCER

Cystectomy or not for Cancer of the Urinary Bladder? Answers to an International Enquiry. Extract from the Journal Urologia. Edited by Prof. Franco de Gironcoli. Pp. 76. Treviso: Libreria Canova. 1956.

Contents: 38 Answers from Italy, France, USA, UK, Eire, Spain, Poland, Sweden, Germany, Greece, USSR, Yugoslavia, Bulgaria, Australia, Argentine Cuba. Results of the Inquiry.

Total cystectomy for cancer of the bladder reached a peak during the decade 1940-50, and since then there has been a marked decline in the popularity of the procedure. Dissatisfaction with the results of uretero-sigmoidostomy has contributed a great deal to this decline and this dissatisfaction has not been dissipated by a consideration of the long-term results as regards cure of the cancer.

Many a surgeon has asked himself whether he is justified in performing so severe an operation and has been led to consider its precise indications and limitations. Franco de Gironcoli therefore sought the opinions of leading urologists all over the world and their replies, with his editorial comments, are published in this number of *Urologia.* As might be expected, there is no unanimity. One group considers that total cystectomy has few indications. A second group consists of those who are still partisans of the operation. The third, and largest, group, recognizing its utility, has endeavoured to state more precisely its now more limited applicability. Among these indications are multiple papillomatosis and growths about the bladder neck which are not suitable for radiotherapy. Some writers even advocate a palliative cystectomy with the object of preventing a 'bladder death'.

This fascinating volume should be studied by every urologist.

J.A.C.

POSTURAL DRAINAGE

Postural Drainage. By Winifred Thacker, M.C.S.P. Pp. viii + 56. 37 Figures. 8s 6d. net. London: Lloyd-Luke (Medical Books) Ltd. 1956.

Contents: Preface. Foreword. 1. Anatomy and Physiology of the Respiratory System. 2. Technique of Postural Drainage. 3. Special Problems. 4. Pre- and Post-operative Treatment. 5. Technique of Breathing combined with Coughing. Appendix.

The need for a working knowledge of the basic principles of postural drainage are emphasized in this little book and acknowledgement is made of the fact that modern physiotherapists play an important part in cases where patients are recovering their lung function after thoracic surgery.

The pictures of positions are set against diagrams of the bronchial tree, and the importance of a knowledge of the anatomy of the 'tree' is stressed. A useful book for nurses who have thoracic cases in their care.

A.T.

VENOUS HAEMODYNAMICS

Venous Return. By Gerhard A. Brecher, M.D., Ph.D. Pp. vii + 148. 55 Figures. $6.75. New York & London: Grune & Stratton, Inc. 1956.

Contents: Foreword, by Carl J. Wiggers. Preface. I. Historical Considerations. II. Elementary Hemodynamics. III. Factors Affecting Venous Return. IV. Present Problems of Venous Return Dynamics. V. Methods for Venous Flow Measurement. VI. Venous Hemodynamics. VII. The Respiratory Pump. VIII. Effect of Artificial Respiration on Venous Return. IX. Effect of the Heart's Action on Venous Return. X. Venous Hemodynamics of Cardiac Valve Lesions. XI. Venous Return During Cardiac Surgery. Final Remarks. Bibliography. Index.

This is the first book since Franklin's monograph on veins. It is also the first book that deals with the physiology of the venous return that has been published since research workers have applied accurate electrical measuring-devices to the study of venous flow.

Dr. Brecher is particularly qualified to have written this monograph since he has made numerous important contributions in this field which have revolutionized some of our concepts of the venous return. It is therefore not surprising that the monograph contains a great deal of original and hitherto unpublished work.

The author's analytic and synthetic approach to the problem of venous return has been made possible by the application of his high-fidelity bristle flow-meter to cogent problems of the venous return.

Although most of the experimental work has naturally been carried out on animals, the clinical application of the results is stressed throughout and there are chapters on the haemodynamic changes in the venous system during open chest-surgery, hypothermia and cardiac surgery.

The problem of the extracorporeal circulation has similarly been submitted to a far-reaching analysis. Thus this book really deals with questions presenting in present-day medical practice and contains valuable information for the clinician and surgeon alike.

Short summaries are provided at the end of each chapter, which greatly facilitate orientation and make it possible to pick out any one of the chapters for special reading.

This book can be recommended, not only to the research worker and physiologist but to the physician and surgeon, with the assurance that they will find an answer to many of their problems and obtain a better understanding of the haemodynamics of the venous system which, as the author points out, to a large extent has been the forgotten part of the circulation.

R.H.G.

CENTENARY OF A LONDON HOSPITAL

The Royal Northern Hospital—1856-1956. By Eric C. O. Jewesbury, M.A., D.M. (Oxon.), M.R.C.P. with a foreword by H.R.H. The Duke of Gloucester, K.G. Pp. xii + 157. 5 Test figures and 23 pp. plates. 17s. 6d. net. London: H. K. Lewis & Co. Ltd. 1956.

Contents: Foreword by H.R.H. The Duke of Gloucester. Acknowledgements. I. The Founder of the Hospital. II. Beginnings at King's Cross (1856-1863). III. The Caledonian Road (1864-1888). IV. The Move of Holloway (1888-1899). V. Development of the Royal Northern Group (1900-1921). VI. Progress and Debts (1922-1939). VII. The Hospital, the War and the National Health Service (1939-1956). Appendix. Members of the Medical and Surgical Staff of the Hospital since its Foundation. Index.

This is a new book published to mark a century of endeavour among the sick poor of North London. The record is fascinating as the growth of the work is traced from its unusual beginnings. The word 'unusual' is employed advisedly; for apparently the use of the adjective 'bloody' by a Junior Assistant Surgeon, Mr. S. F. Statham and the fact that he also, on an occasion, slapped a patient on the bare buttocks led to his expulsion from University College Hospital in 1856 and resulted in the founding by him of the Great Northern Hospital, the forerunner of the present Royal Northern.

Although part of the account of the development is somewhat tedious owing to the frequent references to money in the form of bequests, grants, and dinners and other money-making efforts, one realizes the importance of this commodity in the development of any organization, particularly that of a charity, which it was for the major part of its existence.

The list of medical personalities who have served on the staff of the hospital, which is included in an appendix, includes some famous names in the world of medicine.

A.H.T.

BOOKS RECEIVED : BOEKE ONTVANG

An Atlas of Diseases of the Eye. Compiled by E. S. Perkins, M.B., F.R.C.S. and Peter Hansell, M.R.C.S., F.R.P.S. with a foreword by Sir Stewart Duke-Elder, K.C.V.O., M.A., D.Sc., Ph.D., M.D., F.R.C.S. Pp. ix + 91. Coloured Illustrations. 42s. net. London: J. & A. Churchill Ltd. 1957.

A Doctor Returns. Being the Third Part of 'A Publisher Presents Himself'. By Donald McI. Johnson. Pp. 256. 16s. London: Christopher Johnson Publishers Ltd. 1956.

Endogenous Uveitis. By Alan C. Woods, M.D., with Illustrations by Annette Smith Burgess. Pp. xvi + 303, with XLII colour plates, 81 other illustrations, 8 tables and Bibliography. 100s. 0d. London: Baillière, Tindall and Cox Ltd. 1956.

Tuberculosis control: Plans for intensified inter-country action in Europe. Report of a Study Group. *World Health Organization: Technical Report Series*, 1956, No. 112; 14 pages. Price 1s. 9d., $0.30 or Sw. fr. 1. Also available in French and Spanish. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

Neuroses in General Practice. Being the Second John Matheson Shaw Lecture of the Royal College of Physicians of Edinburgh—Delivered in the Hall of the College on 11 November 1955, by C. A. H. Watts, M.D. Pp. 31. 3s. 6d. Edinburgh: The Royal College of Physicians. 1956.

Animal Diseases in South Africa. Third Edition (Completely Revised). By Michiel W. Henning, M.R.C.V.S., D.Sc. Pp. xv + 1239. 152 Illustrations. £5 10s. 0d. Johannesburg: Central News Agency Ltd. 1956.

Text-book of Physiology and Biochemistry. Third Edition. By George H. Bell, B.Sc., M.D. (Glasg.), F.R.F.P.S.G., F.R.S.E., J. Norman Davidson, M.D., D.Sc. (Edin.), F.R.F.P.S.G., F.R.I.C., F.R.S.E. and Harold Scarborough, M.B., Ph.D. (Edin.), F.R.C.P.E., M.R.C.P. With a foreword by Robert C. Garry, M.B., D.Sc. (Glasg.), F.R.F.P.S.G., F.R.S.E. Pp. xii + 1068. Illustrations (Some in Colour). 60s. net + 2s. 5d. Postage Abroad. Edinburgh and London: E. &. S Livingstone Ltd. 1956.

Pye's Surgical Handicraft. Seventh Edition Fully Revised. A Manual of Surgical Principles, Minor Surgery, and Other Matters connected with the Work of Surgical Dressers, House Surgeons and Practitioners. Edited by Hamilton Bailey, F.R.C.S. (Eng.), F.A.C.S., F.R.S. (Edin.). Pp. ix + 800. 860 Illustrations. 52s. 0d. Bristol: John Wright & Sons Ltd. 1956.

Anatomical Techniques. By D. H. Tompsett, B.Sc., Ph.D. Foreword by Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., F.R.C.S. Historical Introduction by Miss J. Dobson, B.A., M.Sc. Pp. xvi + 240. 83 Figures. 35s. net + 1s. 2d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956.

One Doctor in his Time. By Bethel Solomons, M.D., F.R.C.P.I., F.R.C.O.G., M.R.I.A. Pp. 224. 9 Illustrations. 18s. net. London: Christopher Johnson. 1956.

Cardiology. 2nd Edition. By William Evans, M.D., D.Sc., F.R.C.P. Pp. ix + 574. 569 Illustrations. £5 4s. 3d. plus 2s. 3d. delivery charge. London: Butterworth & Co. (Publishers) Ltd. South African Office: Butterworth & Co. (Africa) Ltd., P.O. Box 792, Durban. 1956.

The British Encyclopaedia of Medical Practice. Including Surgery, Obstetrics, Gynaecology and other Special Subjects. Medical Progress 1956. Editor in Chief Sir Henry Cohen, M.D., D.Sc., LL.D., F.R.C.P., F.F.R. Pp. xiv + 364 + (14). London: Butterworth & Co. (Publishers) Ltd. South African Office: Butterworth & Co. (Africa) Ltd., P.O. Box 792, Durban. 1956.

Schadelijke Nevenwerkingen van Geneesmiddelen. Supplement I. By Dr. L. Meyler. Pp. 127. *f* 9·75. Assen: Van Gorcum & Comp. N.V. 1956.

A Manual of Human Anatomy. Volume I. Thorax and Upper Limb. By J. T. Aitken, M.D., G. Causey, M.B., F.R.C.S.,

J. Joseph, M.D., M.R.C.O.G. and J. Z. Young, M.A., F.R.S. Pp. vii + 162. 36 Figures. 14s. net plus 7d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956.

A Manual of Human Anatomy. Volume II. Head and Neck. By J. T. Aitken, M.D., G. Causey, M.B., F.R.C.S., J. Joseph, M.D., M.R.C.O.G. and J. Z. Young, M.A., F.R.S. Pp. viii + 180. 53 Figures. 16s. net + 7d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956

A Manual of Human Anatomy. Volume III. Lower Limb. By J. T. Aitken, M.D., G. Causey, M.B., F.R.C.S., F. Joseph, M.D., M.R.C.O.G. and J. Z. Young, M.A., F.R.S. Pp. viii + 117. 36 Figures. 12s. 6d. net + 6d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956.

Special Lectures in Biochemistry, 1954-1955. Pp. 106. 36 Illustrations. 12s. 6d. net. University College of London. Distributing Agents: London: H. K. Lewis & Co. Ltd. 1956.

Toxic Hazards of Pesticides to Man. Report of a Study Group. *World Health Organization: Technical Report Series*, 1956, No. 114, 51 pages. Price: 3s. 6d., $0.60 or Sw. fr. 2. Available also in French and Spanish. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

Expert Committee on Insecticides, Sixth Report. *World Health Organization: Technical Report Series*, 1956, No. 110. 88 pages. Price: 3s. 6d., $0.60. or Sw. fr. 2. Available also in French and Spanish. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd. P.O. Box 724, Pretoria.

Surgery of the Hand. Third Edition. By Sterling Bunnell, M.D. Pp. xv + 1079. 1,047 Illustrations and 9 Colour Plates. £7 7s. 0d. net. London: Pitman Medical Publishing Co. Ltd. 1956.

Shaw's Text-book of Gynaecology. Seventh Edition. Revised by John Howkins, M.D., M.S., F.R.C.S., F.R.C.O.G. Pp. vii + 704. 4 Coloured Plates and 352 Text-figures. 32s. 6d. net. London: J. & A. Churchill Ltd. 1956.

Anaesthetics for Medical Students. Third Edition. By Gordon Ostlere, M.A., M.B., B.Chir. (Camb.), D.A. and Roger Bryce-Smith, M.A., D.M. (Oxon.), F.F.A.R.C.S. with a Foreword by C. Langton Hewer, M.B., B.S., M.R.C.P., F.F.A.R.C.S. Pp. viii + 116. 10s. net. London: J. & A. Churchill Ltd. 1956.

A Text-book of Surgical Pathology. Seventh Edition. By Charles F. W. Illingworth, C.B.E., M.D., Ch.M., F.R.C.S. (Ed.) and Bruce M. Dick, M.B., F.R.C.S. (Ed.). Pp. viii + 730. 322 Illustrations. 63s. net. London: J. & A. Churchill Ltd. 1956.

Progress in Clinical Medicine. Third Edition. Edited by Raymond Daley, M.A., M.D. (Cantab.), F.R.C.P. and Henry Miller, M.D. (Durh.), F.R.C.P., D.P.M. Pp. x + 424. 36 Illustrations. 40s. net. London: J. & A. Churchill Ltd. 1956.

Micro-analysis in Medical Biochemistry. Third Edition. By E. J. King, M.A. (McMaster), Ph.D. (Toronto), D.Sc. (Lond.), F.R.I.C. and I. D. P. Wootton, Ph.D. (Lond.), M.A., M.B., B.Chir. (Camb.), F.R.I.C. Pp. xi + 292. 25 Illustrations. 22s. 6d. net. London: J. & A. Churchill Ltd. 1956.

Clinical Examinations in Neurology. By Members of the Sections of Neurology and Section of Physiology, Mayo Clinic and Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minnesota. Pp. xviii + 370. $7.50. Philadelphia and London; W. B. Saunders Company. 1956.

Lehrbuch der Haut- und Geschlechtskrankheiten. Seventh Edition. By Dr. Walther Schönfeld. Pp. xvi + 513. 315 Illustrations. DM 44. Stuttgart: Georg Thieme Verlag. 1956.

Lymphatics, Lymph and Lymphoid Tissue. By Joseph Mendel Yoffey, D.Sc., M.D. (Manch.), F.R.C.S. (Eng.) and Frederick Colin Courtice, M.A., D.Phil. (Oxon.), D.Sc. (Sydney), F.R.A.C.S. (Hon.). Pp. vii + 510. 99 Figures. 60s. net. London: Edward Arnold (Publishers) Ltd. 1956.

Strahlendosis und Strahlenwirkung. Tafeln und Erläuterungen unterlagen für den Strahlenschutz. Second Edition. By B. Rajewsky. Pp. xvi + 364 + 104 Tables. DM 36. Stuttgart: Georg Thieme Verlag. 1956.

Illustrations of Bandaging and First Aid. Fifth Edition. Compiled by Lois Oakes, S.R.N., D.N. (Leeds and London). Pp. vii + 325. Illustrated with 396 Photographs. 12s. 6d. net. + 1s. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956.

The Person Behind the Disease. By Julius Bauer, M.D., F.A.C.P. Pp. vii + 136. 5 Figures. $3.50. New York and London: Grune & Stratton, Inc. 1956.

CORRESPONDENCE : BRIEWERUBRIEK

CORTISONE IN CHRONIC RECURRENT BRONCHITIS OF CHILDREN

To the Editor: Your editorial[1] on cortisone in asthma in the issue of 8 December stimulated me to record my impressions of this treatment in a group of 25 cases of chronic recurrent bronchitis in children. The term asthma is deliberately avoided because it has a serious implication and indicates an apparently incurable disease to parents.

At the outset I would like to point out that the treatment has been used for approximately one year and that the publication of the results is perhaps a little premature. No control group has been followed but the results are far superior to any other treatment I have used over the previous 5 years.

The children treated were between 3 and 14 years of age and had all had frequent attacks of dyspnosia for at least 2 years. Many were seriously disabled and in 5 instances the family had come from Britain because of the child's health. The patients had all received various types of antibiotics antihistamines or vaccines without any prolonged benefit, and the parents were desperate.

The children were treated with a brand of prednisone (a type of cortisone which has a minimal amount of side-effect) antispasmodics and a cough mixture. When considered necessary a broad-spectum antibiotic and vitamins were added.

The children were started on 15 mg. of prednisone daily, which within a few days was reduced to 5 mg. a day and finally to a maintenance dose of 2·5 mg. a day for a period of 6 weeks. The results were dramatic, and in most instances relief was experienced within 24-48 hours and was maintained while treatment was continued and for a further period of 3 months. In 5 instances the improvement was not maintained, even after 3 months' steroid therapy.

The parents were gratified to see that their children appeared to be normal although they realized that it might only be for a limited period. No ill-effects were experienced from the drugs although no special precautions were taken, and in no instance did withdrawal symptoms occur. One 14-year-old girl who had suffered from the disease for 12 years still needs a sedative at night.

In conclusion, I feel that cortisone-like substances have a place in chronic recurrent bronchitis. Exactly how great a place remains to be seen after these cases have been followed up for a much longer period.

Morris Medalie

809 Medical Centre
Jeppe Street
Johannesburg
13 December 1956

1. Editorial (1956): S. Afr. Med. J., **30**, 1179.

‚MENEER' OF ‚DOKTER'

Aan die Redakteur: 'n Mens kom dit dikwels deesdae teë dat 'n chirurg in Afrikaans ‚Mnr.' genoem word in plaas van ‚Dr.' Ek wil graag daarop wys dat dit foutief is. In Engels is dit die gebruik om 'n chirurg ‚Mr.' te noem. In Afrikaans egter noem ons alle geneeshere ‚Dr.', of hulle nou algemene praktisyne of spesialiste is.

R. L. Retief

Privaatsak 221
Pretoria
12 Desember 1956